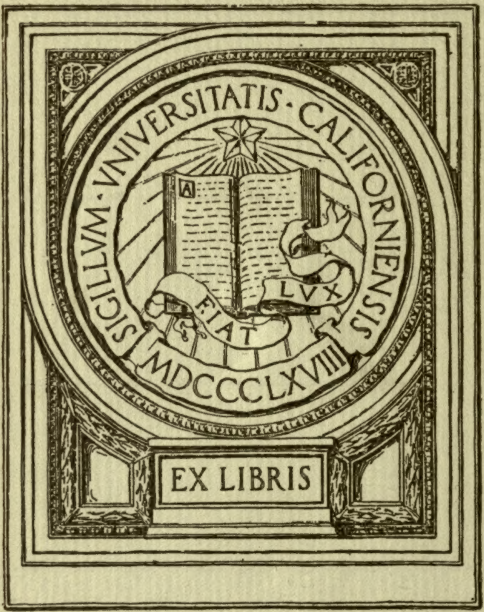
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PHYSIOLOGICAL CHEMISTRY.

3. Green

BY

PROFESSOR C. G. LEHMANN.

11

VOL. III.

TRANSLATED BY

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TABLE OF THERMOMETRIC DEGREES.

C.		F.	C.		F.
—12·5°	=	9·5°	19·4°	=	67°
— 5		23	23		73·4
0		32	24		75·2
2		35·6	28		82·4
3		37·4	30		86
6		42·8	37		98·6
7		44·6	37·5		99·5
8·47		47·2	40		104
13		55·4	43		109·4
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PHYSIOLOGICAL CHEMISTRY.

HISTO-CHEMISTRY.

THE theory of the chemical nature of the animal tissues is a department of physiological chemistry which as yet has been very little cultivated; and the reasons of this unsatisfactory state of our knowledge are too obvious to require any detailed exposition. We will, therefore, simply observe, that the most important obstacle to the chemical investigation of the tissues is, that their elements are too intimately combined or associated with one another to admit of their being prepared for chemical analysis by a previous mechanical separation. This separation of the various elementary tissues which are deposited among, penetrate between, and envelope one another, is rendered the more difficult by the circumstance that with scarcely an exception they are equally insoluble in the ordinary indifferent menstrua employed by chemists. If we have recourse to the stronger or more energetic solvents, as for instance, acids or alkalies, we have seldom any assurance that the dissolved substance is the (otherwise) unchanged histological element, and that the portion remaining undissolved is in reality a simple chemically pure material; indeed, in the majority of cases, there cannot be a doubt that the chemical constitution of the tissue on which we are experimenting is entirely changed by such reagents.

Various means have been attempted with the view of submitting the animal tissues to chemical investigation. The first analyses, having any claim to accuracy, had for their object the determination of the elementary composition; in the Giessen laboratory, Scherer, and subsequently others of Liebig's pupils, instituted elementary analyses of several of the tissues, after purifying them by means of the ordinary indifferent menstrua from any

soluble admixtures that might be present. If in the present advanced state of our knowledge we are compelled to regard such analyses as irrational, since many of the analysed tissues, which were then considered by histologists to be simple, may be now seen by the most superficial microscopic examination to be composed of various morphological elements; yet such investigations must be considered as fully equal to the requirements of science at that date. Chemists were then attaching a high value to the existence of protein, and were striving to ascertain the metamorphoses which it underwent in its conversion into the tissues, and the relations that existed between the chemical constitution of the individual tissues, and the composition of the main constituents of the blood. Moreover, a special value should be attached to these analyses from the circumstance that they form the earliest foundation for the construction of the statistical method, which in the hands of Liebig and others has proved so important an adjunct to chemical physiology. (See vol. i, p. 14.) We should, however, be falling into great error if we were to regard the results of these analyses as strictly accurate expressions of the composition of the tissues in question. The subcutaneous cellular tissue, tendon, horn, &c., are not elementary tissues; for they are composed of various morphological elements, combined together in varying quantities.

This fact induced Mulder to decompose, by means of acid or alkaline solvents, even those tissues which were regarded by histologists as simple; and to attempt to deduce conclusions regarding the morphological arrangement of the various elements or the chemical composition of the original object from the nature of the products of decomposition, by tracing these backwards to their origin. In this manner hair, horn, the nails, tortoise-shell, elastic tissue, &c., were examined either by himself or under his superintendence. Although these investigations led to many interesting results, they did not yield to histologists the information that was expected; for independently of the circumstance that the substances which were examined were not sufficiently defined in their character, and were unfit for an accurate chemical investigation, or even for an exact elementary analysis, the method itself was as imperfect as that to which we previously referred; too little importance was attached to morphologically different constituents of tissues, and hence this method yielded strikingly similar or identical results for very differently constructed (or mechanically composed) objects,—a circumstance which must invalidate the claim of the

chemical analysis to accuracy, and which was itself in part based on the attempt to establish a more intimate ideal connexion between the results of the elementary analyses and the hypothetical formula of the yet more hypothetical protein.

Mulder himself was by no means unconscious of the imperfections of this method, and endeavoured in union with Donders to approach this somewhat inaccessible department of science in a totally opposite direction. The tissues to be examined were exposed to the action of various chemical reagents, and the changes which their texture underwent were observed under the microscope, with the view of deducing from them conclusions regarding the differences in chemical constitution. This course was, however, first adopted by J. Müller, who was led by it to several results of much value in relation to physiology and general anatomy. Several observers followed with more or less success the path which he had thus marked out; but their investigations (unfortunately for us) had reference more to the histological than to the chemical side of the inquiry. Histology has already derived the most important aid from this method, since the reagents which we apply to microscopical preparations are no longer limited to dilute acetic acid, tincture of iodine, or, at most, perhaps a little ammonia. It was by means of microscopico-chemical analysis that the structure of the different horny tissues was first clearly exhibited; who could formerly have established with such precision that nails, cows' horn, and whalebone are composed of aggregations of individual cells, from the most careful tracing of their developmental history? Would the axis-cylinder of the nerve-fibres have remained so long unperceived, or at all events a subject of doubt, if at an earlier period we had been more familiar with micro-chemical investigations? Chemical appliances have often afforded most important service to histology, even when not promoting our knowledge of the chemical constituents of the tissues. We shall, therefore, be warranted in assuming that the progress of histo-chemical inquiry will be satisfactory, when micro-chemical investigation is directed and regulated by the results of micro-chemical analyses; the micro-chemical relations of a tissue serve to indicate the course that must be pursued in order to lead to a successful investigation of the chemical constituents of the tissue, and of its composition.

These are, as we conceive, the points of view from which, in the existing state of science, histo-chemistry ought to be investigated; and in accordance with these ideas, we have attempted to give a sketch of the mode in which it should be treated.

We need hardly remark, in connexion with these histological objects, that the chemist has to deal solely with the elementary tissues; for the coarser or finer admixture of cells, fibres, &c., which we find congregated even in the tissues still deemed simple by many histologists, cannot in themselves constitute the object of a chemical investigation; we should, for instance, regard it as altogether inexpedient to devote special sections of this volume to the consideration of the smooth muscular fibres of the intestine, the contractile tissue of the *tunica dartos*, the middle arterial coat, &c. We know that these tissues are composed of very various histological elements, and that there occur in them, interwoven in many forms and proportions, fibres of connective tissue and nucleated fibres, or ordinary elastic tissue, with the fibre-cells which are common to all contractile organs. The admirable inquiries of Kölliker have indeed shown us that these fibre-cells constitute the most essential element in all the contractile tissues, and his results have been almost as decisively confirmed by chemical investigation as by the certain physiologico-physical test of magnetic electricity, Hence we should not regard the middle arterial coat, or even the walls of the blood-vessels themselves, as subjects for histo-chemical research, but we should rather attempt to ascertain, under the head of "fibre-cells," the chemical character of the substance that is common, and at the same time peculiar, to all contractile tissues. At the present day it would be highly inexpedient to devote special sections to the chemical constituents of the eye, the chemical constitution of the brain, &c. We are, however, as yet unable to limit histo-chemistry very strictly to the consideration of the pure elementary tissues, for we must still speak of nervous tissue, of the striped muscular tissue, &c., although very different morphological and chemical elements are associated in them; for, unfortunately, we have not yet made sufficient progress to enable us properly to distinguish from one another the elementary parts of these compound tissues, and we are consequently obliged to limit histo-chemistry to the mere determination of the chemical characteristics of the morphological elements of the tissues.

Although every one who directs his attention to histo-chemistry must be familiar with the normal histological characters of the tissues, and although every one who would propose engaging in histological investigations must be thoroughly familiar with the present state of general anatomy, we have notwithstanding deemed it expedient to introduce a sketch, short though it may be, of the

conformation of the individual tissues. In accordance with this view, we have endeavoured to indicate, in the shortest possible terms, the morphological relations of each elementary tissue, its admixture with other textural elements, and its occurrence in the various organs of the animal body.

While it cannot be denied that chemical investigations of the tissues, if they are to lead to any valuable result, must be intimately associated with histological examinations, so on the other hand the first step towards a chemical recognition of the textural elements can only be taken through the aid of micro-chemical reactions. We will, therefore, begin the consideration of "histochemistry proper," with a description of the changes which we observe with the microscope in the texture of each tissue after the application of various reagents, limiting ourselves, for the most part, to the results obtained by personal observation. There is no department of physical science in which personal observation is more necessary for the purpose of forming a correct judgment than in micro-chemistry. Our judgment regarding surrounding objects or phenomena, of which we obtain cognizance only through the sense of sight, is exposed to numerous sources of error; we know that in making observations with the microscope we are deprived of many aids which, under other circumstances, would assist us in forming our opinion regarding the objects we perceive, and we especially miss this assistance in forming our judgment regarding the changes which microscopical objects undergo under the influence of chemical reagents; thus, for example, many histological elements swell and become as imperceptible to the eye as if they were actually dissolved, whilst in reality they are simply reduced by the reagent to a gelatinous condition in which their refractive power corresponds with that of the surrounding fluid; and it not unfrequently happens that the membrane or fibre that had become invisible may be again brought into view by repeated washing with water, or by careful saturation of the acid or base that had been employed, thus affording evidence that it had not been dissolved in the reagent. After the application of other reagents, parts often become visible which previously could not be perceived; it is then often impossible to distinguish whether these objects actually existed previously and were only very transparent, or whether they were produced by the application of the reagent. In such cases it is often impossible to arrive at any certain conclusion; we know, for instance, that histologists are not yet fully agreed as to the nuclei which appear so abundantly in the corpuscles

of frogs' blood that has stood for some time, some maintaining that they exist preformed in the fresh circulating blood, and others holding the opposite view.

Again, many reagents induce coagulation of the interstitial juice in mixed tissues, and in this way not only obscure the form, but occasion such contractions and alterations of outline of one or other of the parts, that it often becomes extremely difficult to distinguish to which of the tissues that are thus intermingled the filaments or granules, that are observed, belong. These, and similar relations, make it extremely difficult to form a judgment regarding the effect of the action of chemical reagents on the tissues, and, indeed, often render it impossible to arrive at any definite result. We might adduce many examples of apparently very simple questions regarding which the best histologists are even now at variance (as, for instance, whether nucleoli are or are not contained in the nuclei of certain cells, and whether these nucleoli, when they are unquestionably present, consist of fat or of some other matter). To show that we have not overrated the difficulties of micro-chemical investigation, are there not many who even now deny the pre-existence of an axis-cylinder in the nerve-tubes? and do we not find such distinguished observers as Mulder and Donders holding the apparently very erroneous view that the axis-cylinder visible within nerve-tubes that have undergone change consists essentially of fat?

It is hardly necessary to remark that perfect familiarity with the microscope, and an accurate acquaintance with all the auxiliaries employed in its use, and with all its sources of fallacy, are indispensably requisite for the successful pursuit of micro-chemical investigations. The various means of checking error which have been recommended by such experienced observers as Jul. Vogel,* Schleiden,† Hugo Mohl,‡ Purkinje,§ and others, in ordinary microscopical inquiries, are required in a still higher degree in micro-chemical researches.

It must also be borne in mind that the application of chemical reagents demands the observance of many precautions, the necessity of which has been only recently perceived. Formerly it was the ordinary practice to allow the chemical reagent to flow on the microscopic preparation, and to observe its direct action on the

* Anleitung z. Gebrauch des Mikroskops u. s. w. Leipz. 1841.

† Botanik, Methodol. Einleitung. Leipz. 1849.

‡ Mikrographie u. s. w. Tübingen, 1846.

§ Wagner's Handwörterb. d. Physiol. Bd. 2, S. 411–448.

morphological elements of the object under examination. Donders* has, however, correctly shown that it is very often necessary to submit the tissue we may be examining to the prolonged action of the chemical reagent—an action not merely of hours but of days. We regard both modes of proceeding as absolutely necessary for an accurate examination. In association with Messerschmidt,† I long ago directed attention to the fact, that even in objects which are easily penetrated—as, for instance, pus—the solution of the chemical reagent only very gradually makes its way into the mass of the object, and acts very unequally on the parts that are differently situated; and consequently that the microscopical appearance may often give occasion to very different interpretations. Hence Donders especially recommends that the tissues should not be submitted to microscopical investigation until they have been exposed for a longer or shorter period to the action of the chemical agent in a somewhat disentangled or carefully prepared state. In this way the final result of the action may be much better observed than by any other means, and the altered parts are seen with perfect clearness. In the meanwhile, although the result may be sufficiently obvious, it may often be far from easy to decide in what manner the change has been brought about, and what parts especially undergo solution, contraction, or gelatinisation. If we merely observe such preparations without tracing the action of the chemical reagent upon them under the microscope, we soon see how readily we may fall into error. Hence in every case it is expedient when examining a preparation, at the same time to observe the direct action of the same reagent on it. In the latter proceeding there are various means by which we may be assisted in accurately observing the direct action of the chemical reagent; thus, for instance, Henle recommends that a hair should be introduced between the slide on which the object is placed and its cover, in order to regulate the flow of the test-solution, and to retard its action on the preparation, which is often extremely rapid; linen or cotton threads may often be more conveniently used, provided they are not affected by the reagent. One's own experience is, however, a better guide than any written directions in successfully carrying out experiments of this kind.

Another point of much importance in micro-chemical researches, which has been often neglected even in recent times, and which has been strongly insisted upon by Donders and myself, is atten-

* Holländische Beiträge. 1846, S. 39.

† Arch. f. physiol. Heilk. Bd. 1, S. 225.

tion to the strength of the solutions employed in micro-chemistry. A disregard of this rule frequently led in earlier times to the most discrepant statements regarding the action of various reagents on blood and pus corpuscles, and at the present day we may possibly ascribe to the same cause the very different assertions that have been made regarding the action of various chemical matters on certain tissues. We shall presently see, for instance, what different effects are produced on muscular tissue by extremely dilute, moderately dilute, and concentrated hydrochloric acid, and what different consequences result from the application of alkaline solutions of various strengths to similar objects. Whilst the chemist throws together organised parts, crushes the organic mass in a mortar, and then most laboriously attempts to fish out the individual constituents, always, however, carefully paying attention to his chemical reagents, and the manner in which they should be applied, the micro-chemical inquirer has often followed a totally opposite course; he may have observed the alterations in form which the object has undergone, while he has not sufficiently attended to the nature of the chemical reagents he has employed; indeed, they sometimes seem to be selected at hap-hazard, and are of such a nature that they cannot lead to chemically serviceable results, their application being so irrational in a chemical point of view that, let their action be what it may, no conclusive results can be expected from them. These remarks lead us to another point in micro-chemical analysis, to which we should pay the most serious attention, and by the neglect of which we lose many most important results.

It is obvious that micro-chemical reagents should be applied for other purposes than merely for the object of studying the changes of form which the elementary tissues undergo, and of investigating their minute structure, or of determining whether this or that histological element be the more nearly allied to that hypothetical substance, protein, or whether it rather falls into the very vague category of "gelatigenous tissue," or whether it be altogether different from either. Micro-chemical investigation must be pursued with the same aims as every other chemical manipulation, that is to say, it must be directed to the elucidation of the chemical constitution of the object under consideration, and must indicate the direction to be followed in our advance towards the goal of our inquiries. But this point will not be attained as long as we content ourselves with employing this or that reagent at random, and are satisfied with observing the alteration

of form which it induces, and with ascertaining in what group of chemical substances this or that part of a tissue should be classed. Micro-chemistry must rather furnish us with the means of extracting from the tissue to be examined one chemical constituent after another, and of thus rendering them more accessible to further chemical investigation. We believe that the following pages present some striking illustrations of the advantages of this application of micro-chemistry, which has first indicated the method of investigating the chemical nature of the textures by the separation of the less essential parts interwoven with them; it will thus throw some light on the constitution of parts like the brain, which have hitherto defied all the efforts of pure analysis.

If we glance at the somewhat numerous micro-chemical reactions which have been observed in the different tissues, we shall find that they have rather excited our hopes than fulfilled our expectations. The large number of reagents often scarcely differing in their actions, and their unsystematic accumulation, show clearly enough that this branch of science has as yet been little cultivated, and is but ill adapted to lead us to any explanatory facts. But the cause of the unsatisfactory nature of the efforts hitherto made to advance histo-chemistry by means of micro-chemical experiments, is to be referred less to the inefficiency of our micro-chemical agents, than to the imperfect development of general zoo-chemistry or the theory of the animal substrata. We cannot, however, hope to make great or brilliant progress in the chemical knowledge of the tissues until chemists shall have succeeded in throwing light upon the protein bodies, until better analytical methods are discovered for the distinction and separation of these widely differing, although in some respects analogous substances, or until some more reliable methods can be adopted for the establishment of less hypothetical formulæ than those hitherto employed—as, for instance, in the case of albuminous substances. The protein hypothesis has frequently served as the *πρῶτον ψεῦδος* for giving scope to hazardous conjectures on the nature and formation of the tissues, as well as on the entire metamorphosis of matter in the animal body. We have, therefore, abstained as far as possible from giving the artificial formulæ and equations by which it has been attempted to exhibit an ideal connexion between the composition of the different tissues and their origin and metamorphosis, since it appears to us that science in its present undeveloped state more especially demands caution in the indulgence of fanciful hypotheses. A cautious reserve in this respect is more especially

called for from those pathologists who imagine that a pathological histo-chemistry may be hurriedly built up on a few insecure props, and who have obscured the few exact chemical facts which we possess regarding morbid tissues with their own nebulous hypotheses.

If, however, we would extend to histo-chemistry our inherent tendency to general abstractions, we may consider the general proposition (laid down in vol. i, p. 25), that the physiological importance of a substance is dependent on its chemical constitution, as being equally well established, in so far as our experience goes, in regard to the tissues; for we merely express the simple result of positive experience, and the inductions deduced therefrom, when we assert that *the chemical nature of the tissues invariably corresponds with their functions.* It has been long known that those tissues which are of service in the animal body almost solely from their physical properties (their hardness, toughness, elasticity, &c.), contain as their most essential basis a substance which on boiling yields gelatin; we further know that those textural elements which are remarkable for a high degree of elasticity, as the nucleated fibres of connective tissue and the true elastic tissue, present a perfectly similar chemical relation; and as we gradually develope the subject of histo-chemistry, we shall have convincing evidence that those tissues which exhibit special vital activity—those, namely, which, in addition to a slight but very perfect elasticity (Ed. Weber), possess the power of contracting in consequence of certain influences transmitted through the nerves—contain, as a matrix and essential constituent, one and the same substance, muscle-fibrin or syntonin; here we must place the fibre-cells of those tissues which are specially known as "contractile," and of smooth muscle, and the cylindrical fibres of striped muscle. The arrangement and the chemical character of the substrata constituting the nervous system, confirm rather than oppose the above proposition, and afford a new proof that the material substrata of the tissues are always constructed in chemical conformity with their vital functions.

There is one more circumstance which must not be left altogether unnoticed, and which probably stands in a nearer connexion with the above subject than might at first sight be supposed; we refer to the fluids permeating and bathing the tissues. We have already seen that there are great differences in the chemical character and composition of the fluids moistening the different classes of tissues, the peculiarities of the fluid being apparently

closely connected with the chemical constitution of each individual tissue. We find, for instance, that the lower elementary tissues, such as exert a mere physico-mechanical action, are moistened by a fluid which scarcely differs from the serum of the blood, and in general closely resembles the transudations described in the second volume. On the other hand, the tissues which are capable of a vital contraction, and, consequently, the fibre-cells and muscular fibres, are surrounded by a fluid which is altogether different from an ordinary transudation; in the first place this fluid is distinguished, in all contractile tissues without exception, by the presence of a certain amount of free acid; further, the phosphates and potash-salts predominate here over the chlorides and soda-salts (which preponderate in the transudations); and, lastly, there occur in this fluid a number of substances which, hitherto at least, have not been recognised in the blood and transudations. It may probably depend upon the different modes of action of the fibre-cells (in the contractile tissues and in smooth muscles) and of the muscular fibres (in the striped muscles), that the acid interstitial juice in the former case always contain casein with albumen, whilst, in the latter case, it contains no casein, but several other substances peculiar to itself alone. Unfortunately these relations afford us as yet mere points of view from which we may get glimpses of the connexion between the chemical composition and the function of the tissues, or at most a few new advanced points from which we may hope by further investigations to promote the physiology of the animal tissues.

The preceding remarks will sufficiently elucidate the course which we intend to pursue in treating of the chemical relations of the animal elementary tissues. We first notice the *micro-chemical reactions.* In the present very imperfect state of micro-chemistry a logical arrangement and subdivision of these reagents is out of the question, and hence their number is far greater than it would otherwise be. Although many of these reagents act in a very analogous manner, and others again do not yield very definite results, we shall, nevertheless, mention them in detail, as we are of opinion that in a rapidly advancing and comparatively new department of science every fact, however unimportant, should be retained, since we do not know what significance it may subsequently attain. Moreover, no accumulation of facts can do harm.

Basing our remarks for the most part on the micro-chemical reactions, we shall next proceed to the investigation of the chemical properties and composition of the individual substances which may

be extracted or isolated from the tissues, without any essential change in their composition. We shall then notice the parenchymatous juices which permeate the tissues, provided they exhibit any peculiar chemical relations. Without entering deeply into the purely physiological relations of the individual tissues, we shall then consider the question whether anything definite, regarding the physiological function of the tissue, can be deduced from its chemical constitution, in so far as it is yet known.

Finally, we shall endeavour, at the conclusion of each subject, to form, as it were, a basis for an introduction to a more general chemical analysis from the results obtained by the micro-chemical investigations. If our previous remarks on the chemistry of the tissues have failed to demonstrate the great deficiency of our knowledge in this department, the analytical results will afford conclusive evidence that we are still very far from being able to clothe histochemistry in a rational garb, or to represent in a scientific form the morbid changes of the tissues.

Osseous Tissue.

Were we to consider the constitution of osseous tissue only from a chemical point of view, without reference to its histological conformation, we should scarcely arrive at anything like a correct idea of bone. We must, in the first place, bear in mind that this substance, which was formerly included amongst the simple tissues, has not only a somewhat varying, but also a complicated texture, in which, as in the tissues of a higher order, vessels and nerves enter, and in which, as in other tissues, nutrient matter (or plasma) and effete materials are met with. Without entering minutely into the structure of osseous tissue, we must at all events remark that this substance—whether pertaining to the flat or the long bones—is penetrated by numerous cavities and canals which, in the fresh bone, are not empty, and, in the dry, contain at least the non-volatile constituents of the former contents. These cavities in the bones are not merely those which are perceptible to the naked eye, as for instance, the great medullary canal in the centre of the cylindrical bones and the cellular spaces of the spongy bones, and the nutritious foramina; in addition to these more obvious solutions of

continuity, there are two different kinds of minute canals, one being much smaller than the other, and both perforating the true osseous substance. The larger of these sets of tubules, which have an average diameter of 0·01—005‴ (Kölliker),* and are known as the Haversian canals, or *canaliculi medullares,* form a net work in the more compact osseous tissue, and open (1) externally on the outer surface of the bone, and (2) internally, on the walls of the medullary cavities and spaces. The substance, however, which is surrounded by these spaces, is by no means to be regarded as the matrix of bone—as a perfectly continuous tissue, for we find in it a third group of tubules by which the bone is converted into a thoroughly porous substance. It is these tubules which were formerly regarded as the special morphological elements of osseous tissue, and were known as the bone-corpuscles and *ductuli chalecophori:* they are empty spaces, which, on examining dried sections of bone under the microscope by transmitted light, are such conspicuous objects from their black colour, or rather their opacity. These elongated lenticular bone-cavities, which have, according to Kölliker,† an average length, breadth, and thickness of 0·01‴, 0·004‴, and 0·003‴ respectively, send out innumerable intercommunicating off-shoots (the above-mentioned *ductuli chalecophori*), and convert the matrix of the bones into a most porous material.

All these cavities, which we find in macerated and dried bones, are filled in fresh bones with various tissues and materials which do not pertain to the osseous matrix—the true object of chemical examination. It is well known that the large cylindrical cavities of the tubular bones are filled with marrow, of which we shall speak presently; this marrow is also found in the cancelli of the apophyses of the cylindrical bones, and in the cavities of the spongy substance of the flat and short bones, but is not contained in the dense cortical substance; hence it does not penetrate into the Haversian canals, which only exist there. While the marrow consists of a little connective tissue, and some vessels intermingled with the true medullary matter, the Haversian canals contain only blood-vessels and the nerves pertaining to them.

With regard to the bone-corpuscles and their prolongations, it was held, until very recently, that, as their name indicated, they consisted essentially of calcareous salts, or, at all events, were filled with them. This error, which was first exposed by Bruns

* Mikrosk. Anat. Bd. 2, S. 278.

† Ibid. Vol. 2, p. 291.

and Bowman, and afterwards more fully by Kölliker, was one into which it was the more easy to fall, because, on the one hand, these air-containing spaces refract the light in its passage from the osseous matrix into these cavities in such a manner that these parts appear perfectly dark in consequence of the deviation of the rays, and thus resemble opaque objects, such as we often find (in another form) in morbid concretions, and because, on the other side, it is only with difficulty and by a very slow process that these empty spaces and passages can be filled with fluids. (The best fluids for this purpose are the oils and balsams.)

Virchow and Donders, and more recently Hoppe,* have shown the extreme probability that these bone-corpuscles and their prolongations are not simple excavations in the bone, but that they are lined by a membrane, by finding that after the prolonged ebullition of pieces of bone (the tegumentary bones of the sturgeon) the corpuscles, with their prolongations, remained perfectly intact after the solution of the matrix. Drummond† maintains, as Kölliker had previously done, that a nucleus is constantly present in the bone-corpuscles.

The easiest method of demonstrating that the bone-corpuscles and their prolongations are cavities, is to apply a little pure turpentine or Canada balsam to the edge of a long thin slip of bone (which, after perfect drying, serves the best to exhibit these parts) and to examine it under the microscope; we then perceive the dark bone-corpuscles and their prolongations very gradually become light, by slowly absorbing the turpentine, and thus losing their strong refractive power.

These minutest cavities or pores do not contain air in the fresh moist substance; they must be filled with a fluid whose refracting power is not very different from that of the matrix of bone, as is obvious from the investigation of fresh or thoroughly moistened osseous tissue; hence a deposition of calcareous salts within them is out of the question. No examination has as yet been made of the contents of these pores and cavities in fresh bones; it must, however, suggest itself to every one, that this system of most minute cavities which communicates on all sides with the Haversian canals (the vascular cavities of the bones) must take up the transudations from the vessels (the nutrient fluid) and reconvey the effete particles in a state of solution into the Haver-

* Arch. f. pathol. Anat. Bd. 5, S. 176.

† Monthly Journ. of Med. Science. Vol. 14, p. 285.

sian canals. If we could succeed in collecting the contents of these minute tubes in a state of purity (which is by no means impossible), we should thus have an opportunity of chemically examining a perfect physiological plasma.

We perceive, from this short notice of the different systems of cavities which penetrate bone, and of the variety of their contents, that even in analysing bones that have been long and carefully macerated, we are dealing with not only the true osseous substance, but with other matters, as, for instance, the remains of the contents of the various canals, &c.

But before proceeding to the chemical consideration of the bones, we have still to determine the question whether the true matrix (independently of the contents of these canals) is a thoroughly homogeneous mass, that is to say, whether, morphologically considered, it exhibits a perfectly homogeneous continuity, and whether in a chemical point of view, it can be regarded as a perfectly uniform material, that is to say, as a chemical compound of certain proximate constituents.

The matrix of bone is found on a careful microscopical examination to be far from perfectly homogeneous. In the first place, on examining well-prepared transverse sections, we perceive a number of concentric circles surrounding the section of each Haversian canal. These circles are true lamellæ, varying in thickness from 0·002 to 0·005‴ (Kölliker).* Besides these lamellæ connected with the Haversian canals, there is also a general system of such plates which correspond to the outer and inner surface of the bone, and are parallel to these surfaces. (Kölliker's Fundamental Lamellæ.) Associated with these and interspersed here and there in the interior of the bone between the lamellæ of the Haversian canals, are isolated groups of parallel lamellæ. (Kölliker's Interstitial Lamellæ.) These are most distinctly seen in sections of bone that have been carefully treated with dilute hydrochloric acid; but they may also be recognised in incinerated bone. But even the individual lamellæ, independently of the very minute tubules occurring in them (the bone-corpuscles with their prolongations), are not by any means homogeneous: we remark in them an extremely fine punctated appearance, depending on the presence of innumerable pale granules of nearly uniform size (according to Kölliker, about 0·0002‴). Kölliker is inclined to regard these granules as identical with the angular corpuscles which Tomes found in the fragments of

* Mikrosk. Anat. Bd. 2, S. 288.

incinerated and crushed bone, and he considers it not improbable that the true osseous tissue, or the matrix of bone, consists entirely of an intimate admixture of granules firmly combined with one another. If this supposition should be confirmed by further investigations, we could hardly conceive a juxtaposition of these granules without an intervening substance: and even if this view regarding the minute structure of osseous tissue should not be confirmed, the granular appearance would always militate against the homogeneity of osseous tissue.

The chemical, like the physical relations of osseous tissue, indicate that in the minutest particles of it there is a very intimate blending of the textural elements, but not a true mixture (or chemical combination) into a homogeneous substance. It may be inferred from the results of Hoppe's experiments, to which we have previously referred, that the bone-corpuscles and their prolongations are invested by an albuminous membrane insoluble in boiling water.

Further, it is an old-established fact that almost all the earthy constituents may be extracted by dilute acids from a bone, without affecting its form, or even destroying its minute structure; in the same way the form and structure of a bone remain unchanged when we remove the organic matter from it, either by calcination or by careful boiling with dilute alkalies. These two facts might at first seem to be in favour of the view that the osseous tissue is homogeneous, and that there is an actual chemical combination between its organic and inorganic matters; but when we consider that the very numerous analyses of bone which have been already published do not lead to the inference that there is a definite proportion between the organic and inorganic matters, but on the contrary, that the proportions vary extremely in accordance with the physiological conditions,—and further, when we bear in mind that the cartilage may be removed from bone even by the weakest agents, as for instance, by boiling with water in a Papin's digester, or by an extremely dilute solution of potash,—we feel at all events that we have grounds for doubting that the matrix of bone is a chemical compound of earthy and organic matters; and we are strengthened in these doubts by observing that the minute points grow pale or entirely disappear in osseous substance treated with dilute hydrochloric acid.

As we have already spoken, in the first volume, of the individual constituents of osseous substance, we need here only observe in reference to its qualitative composition, or rather, in reference to

that of bones in general, that the most essential organic constituents are gelatigenous cartilage (vol. i, p. 396) and fat (vol. i, p. 249), while the inorganic are phosphate of lime (vol. i, p. 412), phosphate of magnesia (vol. i, p. 422), carbonate of lime (vol. i, p. 418) and fluoride of calcium (vol. i, p. 424). In addition to these main constituents, the bones also contain substances which must be regarded as incidental or unessential constituents of osseous substance. Thus the alkaline sulphate in Bibra's cases* (see vol. i, p. 444) should probably be regarded as for the most part the product of the incineration of the bones. With regard to the other soluble salts that can be extracted by water or spirit from fresh pulverized bones after the removal of their fat, we possess no investigations which enable us to decide the question whether the chloride of sodium, carbonate of soda, &c., are at all events in part peculiar to the matrix of bone, or whether they only belong to the blood which can never be thoroughly removed, or to the fluid contents of the bone-corpuscles and their prolongations. Precisely the same may be said of the organic substances which may be extracted from pulverized bone by digestion with mere water, or more thoroughly (together with the earthy salts) by dilute hydrochloric acid. Even the fat which we have enumerated amongst the main constituents can only occur in extremely small quantity in the matrix of bone. For the small quantity of fat (from 1 to 3%) which we find in bones that have been as thoroughly as possible cleaned and macerated, must be chiefly marrow from the cavities of the spongy portions of the bones, and only a mere trace can arise from the matrix: we, moreover, find from the investigations of the most distinguished histologists, that the marrow does not pass into the Haversian canals of the compact osseous substance. Hence it is only by the analyses of bones which have been well macerated and deprived of their fat that we can hope to arrive at any definite conclusion regarding the constitution of the osseous matrix.

The bone-cartilage, obtained by prolonged digestion with dilute and frequently changed hydrochloric or nitric acid, occurs in its moist state as a tolerably elastic, yellowish, translucent substance, which perfectly retains the form of the portion of bone from which it was obtained. When dried, it becomes very hard, but only slightly brittle. When it has been so often extracted with a weak acid solution that the latter no longer exhibits any traces of dissolved lime, the cartilage leaves very little or a mere trace of ash on incineration. We have already mentioned that neither Marchand

* [See the foot-note in page 21.]

nor von Bibra could recognize any difference between the elementary composition of this cartilage and of the glutin obtained from it or from tendons or connective tissue. The analyses of thoroughly pure bone-cartilage and of glutin coincide so accurately with one another, that notwithstanding their somewhat high atomic weights, we must regard these substances, if not isomeric, at all events as polymeric, although we always find a little sulphur in the former, which is absent in the latter. Bibra* has made the interesting observation, that in fossil bones in which the organic substance is still retained, the cartilage is converted into a glutin-like substance or into true glutin. After freeing these bones in the ordinary manner from their earthy constituents, it was found that the residual cartilage fused at a temperature at from 37° to 40° into a thoroughly gelatinous mass, which swelled up in water into a trembling jelly. This only took place, according to Bibra, in true fossil bones, and not in those which were obtained from ancient graves. We shall postpone the description of the characters of the cartilage which occurs in bones before true ossification takes place, till we treat of cartilage generally. Neither Bibra†, Ragsky,‡ or any other chemists have found any essential alteration in the cartilage of diseased bones; in all cases the cartilage was converted by boiling with water into a substance perfectly similar to glutin.

As we have already described in considerable detail (in the first volume) the individual mineral constituents of bones, and the varying quantities in which they occur, we shall here merely present the reader with a general scheme representing the constitution of compact osseous tissue, as deduced from the best analyses:

Phosphate of lime . . .	57
Carbonate of lime . . .	8
Fluoride of calcium . . .	1
Phosphate of magnesia . .	1
Mineral constituents . . .	67
Cartilage	33
	100

The fluctuations in the proportions of the individual constituents are by no means inconsiderable under different physiological

* Chem. Untersuch. über die Knochen u. Zähne. 1844, S. 399.

† Op. cit. p. 319.

‡ Rokitansky's Handb. d. pathol. Anat. Bd. 2, S. 205 [or English Transl. Vol. 3, p. 182].

conditions, as has been already shown in the first volume. The differences which the different bones of one and the same individual exhibit are especially interesting. Von Bibra has especially elucidated this point by the most conclusive results. With regard to the proportions between the organic and inorganic matters, Rees has, next to Bibra, most distinctly shown that the bones of the extremities are in general richer in earths than those of the body; of the former the humerus and femur contain somewhat more than the other cylindrical bones; the cranial bones contain about the same quantity of earths as the cylindrical ones, while the metatarsal and metacarpal bones have a closer affinity in this respect to the bones of the trunk. The ribs and the clavicles contain on an average rather more organic substance than the vertebræ; those of the pelvis approximate very closely in this respect with the last-named bones. The carbonate of lime appears to be entirely dependent upon the quantity of the phosphate of lime in the different healthy bones of the same individual; at all events, Bibra found that in the most diverse bones of the same animal, the carbonate and phosphate of lime always stood in nearly the same ratio. Moreover, it would appear from the observations at present in our possession, that the quantity of magnesia in the different bones rises and falls with that of the phosphate of lime. The short bones always contain, according to von Bibra, more fat than the cylindrical bones, even where the former have been as completely as possible freed from spongy substance. The quantity of water contained in the bones has been made the subject of special investigation by Stark*: it cannot generally be determined with much accuracy, but Stark's observations show that the flat bones contain more water than the cylindrical (probably from the former being the more vascular).

Although the female skeleton is on an average far lighter than that of man, the comparative analyses of the same bones of both sexes show very trifling, and, as it would appear, altogether unessential differences. If we may be allowed to assume (with physicians) the existence of a certain predisposition, we would say that it would appear from the various recorded analyses of morbid bones, that the female bones more readily undergo a loss of earthy constituents than male bones, or to speak more correctly, that processes which contribute to the absorption of bone-earth are more frequently developed in the female than in the male organism.

* Edin. Med. and Surg. Journ. Vol. 163, pp. 308–325.

It has been found that in man as well as in the other mammalia and in birds, the bones in youth, especially in the human race, contain less earthy constituents than those of adults, but that in advanced age, the bones are universally richer in earthy or mineral matters (Thilenius, Davy, Schreyer, Frerichs,* von Bibra). We cannot decide from the facts in our possession whether the diminution of the earthy matters, which has been often observed in the bones of aged persons, is dependent on physiological or pathological causes. Different observers have arrived at very different conclusions regarding the ratio of the carbonate to the phosphate of lime at various periods of life. It has been already stated (vol. I, p. 419) that I found far more carbonate of lime in proportion to the phosphate in the bones of a new-born child, than in those of an adult and of an old man, while von Bibra found on an average far less carbonate of lime in the bones of young animals. Moreover, von Bibra found rather more phosphate of magnesia in the bones of several very young animals than in the corresponding bones of those that were older. The period of life exerts, according to Bibra, no essential influence on the amount of fat in the bones.

It can hardly be doubted that the food must exercise some influence on the constitution of the bones—a view which seems proved, not merely by the experiments of Chossat and von Bibra,† (referred to in vol. I, p. 413), but also more especially by the investigations of the latter observer on the bones of different classes of animals.

It appears from the numerous investigations of von Bibra and Stark on the effects of different kinds of food on the bones of the *mammalia*, that the amount of cartilage remained unaffected, but that essential differences were induced in the composition of the inorganic constituents. The bones of the herbivora contain on an average rather more carbonate of lime than those of the carnivora; the bones of the pachydermata and cetacea were found to be especially rich in this salt by von Bibra (who always used the femur in these comparative analyses). There seems to be no perceptible difference in the amount of fat in the bones of the carnivora and herbivora; von Bibra, however, found that the bones of horses contained very much more fat than those of other animals. The bones of fat animals usually contain more oily

* Ann. d. Ch. u. Pharm. Bd. 43, S. 251.

† Op. cit. p. 47.

matter than those of lean ones, and hence the bones of hybernating animals contain considerably more fat before than after their winter-sleep. According to Stark, human bones are richer in water than those of any other mammal.

Von Bibra almost invariably found more bone-earth in the bones of *birds* than in those of mammals. The rasores were the richest in mineral substances (the mean being 75·8%; in Columba Turtur the earthy matter rose to 84·3%). The bones of carnivorous birds are generally only slightly richer in earthy salts than those of mammals. The ratio of the carbonate of lime to the phosphate is generally greater in the bones of birds than in those of mammals. There is, on an average, rather more fat in the bones of birds than of mammals, and the granivorous, and especially the aquatic birds, in this respect exceed those living on flesh. According to Stark, the bones of birds contain more water than those of mammals. Moreover, the bones of granivorous birds contain rather more silica than other bones.

Stark has also instituted comparisons between the organic and inorganic substances in the bones of mammals and birds, but his results are not in accordance with those of von Bibra. In all probability, the osseous substance had not been perfectly dried in most of Stark's comparative analyses.

Our knowledge of the composition of the bones of the *amphibia* is almost entirely due to the labours of von Bibra. These bones contain an average less inorganic matter than those of mammals and birds (those of the Salamandrida, for instance, only 55%, and those of the frog 63%); moreover, the ratio of the carbonate of lime to the earthy constituents generally, is less in the bones of the amphibia than in those of the preceding classes. As has been already stated in vol. I, p. 444, von Bibra found a considerable quantity of sulphate of soda* in these bones.

The bones of *fishes* are poorer in mineral constituents than those of any of the preceding classes (the earthy matters varying from 21 to 57%). Although, with regard to the earthy salts, the carbonate of lime appears to a certain extent to rise and fall with the phosphate, no definite proportion can be detected as existing between them. As in the case of the amphibia, von Bibra found that these bones contained more sulphates and fat than those of

* [The Editor regrets to find that a rather important *erratum* escaped his notice in correcting the page referred to in the text. In line 8 from the bottom of page 444, read "sulphate of soda" in place of "soda."]

mammals or birds. According to Stark, the bones of fishes contain more water than those of any other animals.

Notwithstanding the enormous number of analyses of *morbid bones* which have been made by different chemists, very few results with any claim to certainty have been obtained regarding the composition of the bones in definite diseases. To this unfortunate circumstance we must in a great measure ascribe the difficulties which present themselves in diagnosing diseases of the bones during life, and often even after death, if we regard the diseased bone merely as an isolated pathologico-anatomical specimen. We need only refer to the osteomalacia of children (rachitis) and of adults, to the different kinds of osteoporosis, to primitive and consecutive scleroses, to the various osteophytes and ivory-like exostoses, &c. It appears to be often difficult, without a previous knowledge of the mode in which the bone-disease was developed, to give a decided opinion on its nature, even when it is brought before us as a piece of morbid anatomy. We are, moreover, inclined to believe, without in any way criticising the anatomical observations hitherto made in connection with diseases of the bones, that the whole subject requires further development in a pathologico-anatomical point of view. The chemist must therefore be pardoned if (as has more than once happened) he should mistake osteoporosis for osteomalacia, if he should regard an osteopsathyrosis as softening of the bones, and not as a subdivision of osteoporosis ; in short, if in many cases he should confound osteoporosis with osteomalacia, and rachitis with caries. It is no wonder, then, if in the analysis of osteoporotic bones we rarely or never ascertain whether the rarefaction of the osseous tissue depends upon a simple syphilitic, arthritic, or tuberculous ostitis, or on an excessive growth of medulla, or on simple atrophy of the bony tissue; that is to say, upon the disappearance of the above-mentioned concentric osseous lamellæ from the Haversian canals. Nor need we wonder that we are yet so comparatively ignorant regarding the chemical constitution of the osteoscleroses ; for excepting the analyses of Ragsky,* von Bibra,† Schlossberger,‡ Gerster,§ Gruber and Baumert,||

* Rokitansky's Handb. d. pathol. Anat. Bd. 2, S. 201–205 [or English translation, Vol. 3, pp. 180–182.]

† Arch. f. phys. Heilk. Bd. 6, S. 287–299.

‡ Ibid. Vol. 8, pp. 69–87.

§ Ibid. Vol. 6, pp. 142–146.

|| Beiträge z. Anat. Physiol. u. s. w. 2 Abth. Prag. 1847.

C. Schmidt,* and C. O. Weber,† we find very few chemical investigations accompanied with a history of the disease under which the patient laboured. In the absence, therefore, of an accurate history of the case, we can ascertain very little from our numerous analyses of morbid bones, seeing that in the great majority of cases only very unimportant differences are apparent in the composition of very differently named morbid bones. Moreover, such different methods have been employed in preparing the bones for analysis, and in conducting the examination, that the results that are obtained do not admit of comparison.

On entering upon the special examination of the results of these numerous investigations, we have, first of all, to notice the general proposition enunciated by von Bibra, that in almost all morbid processes implicating the bones the mineral substances are abstracted from the tissue earlier and in larger quantity than the organic matter; and that in almost all diseased bones a relative increase of the cartilage is observed. The bone-earth is not only earliest separated from already formed bones during morbid conditions, but it is also last deposited in the bones after the cessation of disease, as, for instance, is seen in the composition of the scleroses; for a bone, or a part of a bone, often exhibits the most decided physical characters of sclerosis when the earthy constituents are far below the normal average. It is an error to suppose that in sclerotic bones there is more earthy matter and less cartilage than in normal bones. This much only is true, that in consecutive sclerosis, that is to say, after osteoporosis or osteomalacia the bone gradually recovers its earthy constituents, although not always to such a degree as to reach the normal proportion between the inorganic and organic matters. At all events, the analyses of Ragsky and Baumert do not prove more than this.

The *cartilage* is very rarely affected in morbid bones. Most observers have obtained the ordinary glutin from the cartilage of diseased bones. (In some cases of very decided rachitic bones both Marchand and I have failed to obtain any true glutin.)

The amount of *fat* in the bones has only been accurately determined in a few cases; but von Bibra's analyses lead to the inference, that generally when, in consequence of disease, a bone has suffered a loss of earthy matter, and still more of its cartilage, the quantity of its fat is increased.

* Ann. d. Ch. u. Pharm. Bd. 61, S. 329.

† Commentatio præmio ornata. Bonnæ, 1851.

A very important question forces itself upon our notice in considering the diseases of the bones, namely, whether there are constant changes in the *relative proportions of the mineral constituents*, and especially whether, when there is resorption of the bone-earth, the strongly basic phosphate of lime is replaced by a less basic salt. Unfortunately most of our analyses of morbid bones are not of such a nature as to enable us to elicit from them even a probable answer to this question. How seldom, after the bones have been properly prepared for analysis, has it been attempted to ascertain the quantity of carbonate of lime in the fresh bone, or in the earthy constituents, by the direct determination of the carbonic acid! Indeed, in most analyses, the older method of Berzelius for the determination of the phosphate of lime has been employed, according to which we could never be certain whether we were weighing $8CaO.\,3PO_5$ or $3CaO.PO_5$. We shall presently notice the reasons why this and similar questions are not so easy to answer as might at first sight be supposed. It appears, from the analyses in our possession, as if the carbonate of lime first diminished and subsequently again increased in a corresponding proportion with the phosphate, in diseases of the bones; it is only in osteophytes and new formations of bone that we frequently find the carbonate of lime exceeding the normal standard.

After the preceding observations, it would scarcely seem necessary to consider the composition of the bones in reference to the ordinary nosological classifications; we must, however, attempt this course, partly to show how deficient our knowledge on this subject is, when we cease to be contented with abstract diagnoses or mere nominal designations, and attempt a more scientific mode of consideration, and partly also to demonstrate that unless we implicitly follow the leading maxims afforded to us by pathology, little real advance can be made in this department.

If we follow the method of inquiry at present pursued in pathology, which refers almost all anatomical changes of the tissues and organs to a so-called inflammatory process, we must begin by studying the chemical changes which are coincident with the textural alterations of the bones that are induced by an ostitis, a periostitis, disease of the medulla, &c. But when we see the results of an ostitis exhibiting themselves in various ways, according as it depends on purely local causes or on specific or general diseases, or as it attacks this or that group of bones, we may at all events conclude, *a priori*, that even where the textural changes are nearly the same, the chemical constitution of the altered bones need not be similar

or even analogous. Thus it is easy to form a conception of osteoporoses whose origin might be dependent on such different morbid affections that according to the different diseased condition from which they arose, they must have a thoroughly different chemical composition, although morphologically they might be extremely similar. This is shown in a certain degree by the analyses which we at present possess of osteoporotic bones, although these investigations are far from being altogether satisfactory; and seems most decidedly established in the case of caries. Adopting the view held by morbid anatomists, that inflammation of the bones terminates in hypertrophy, we have three kinds of hyperostoses to consider, which morphologically, and in part also chemically, differ from one another, namely, primary sclerosis, osteophyte, and exostosis.

We possess two analyses, made by Ragsky, of *primary sclerosis*, whose occurrence is generally supposed to depend upon the gradual conversion into cartilage, and finally into bone, of an exudation within the medullary cavities and the Haversian canals (by which the osseous tissue becomes condensed and almost ivory-like); they do not, however, at all indicate an augmentation of the mineral constituents of the bones. Even in true sclerosis there is never an excess of earthy matter in proportion to the organic substance deposited in a bone, and hence, we cannot suppose that in primary sclerosis such an augmentation of the mineral substances should occur. When the exudation is transformed into osseous substance, this newly formed structure must at first contain less mineral matter than true bone, and on this account, as indeed is completely in accordance with the analyses, it happens that we often find a relative diminution of the earthy matters in sclerotic bones as compared with normal osseous tissue. All that we can deduce from our analyses of such bones is, that on the one hand their organic basis differs in no respect from the ordinary gelatigenous cartilage, and that on the other, there is a considerable augmentation of the carbonate of lime in proportion to the phosphate.

As *osteophyte* is a new formation of osseous substance on the surface of bone, its composition must naturally vary very considerably with the length of its existence, that is to say, with the stage of development into which it has entered from the period of the original formation of the exudation. In the majority of cases both of puerperal and other osteophytes, it has been found both by Kühn and myself, that there has been an excess of organic substance and of carbonate of lime above the normal mean. As in callus

(according to Valentin), so also in osteophyte, there is more carbonate of lime than in those products which are more similar to osseous tissue. No attempt has been made to ascertain whether in the early stage the cartilage yields chondrin on boiling, as is the case in callus and bones previous to ossification; but gelatigenous cartilage is contained in perfectly ossified osteophytes.

The analyses of *exostoses* lead to the same conclusions as those of osteophytes (Lassaigne).

Osteoporosis, which is a dilatation of the medullary cells, and of the Haversian canals, may also be the result of inflammation of the bones, since the exudation that is deposited induces a resorption of the lamellæ, and consequently a rarefaction of the tissue. But, according to Rokitansky, osteoporosis may also result from excessive development of the medulla, which then penetrates the canals, dilates the cavities, and thus increases the volume of the affected bone. Finally, osteoporosis may arise in consequence of old age or of certain *dyscrasiæ* (arthritis, syphilis, &c.,) through simple atrophy with resorption of the lamellæ surrounding the canals, and it then yields an extremely brittle product (osteopsathyrosis). In the chemical investigation of bones that have undergone rarefaction (or expansion) these three conditions must not be overlooked; in all previous investigations, however, little or no attention has unfortunately been paid to these differences. Analyses of porous bones have shown nothing beyond the fact that in general the resorption of the mineral matters of the bones, even in osteoporosis, proceeds more abundantly than that of the cartilage, and that the cavities which have been produced are filled sooner or later with fluid fat. It has been inferred from these analyses, that the carbonate of lime is resorbed in relatively larger quantities than the phosphate; but it is only in a few analyses that this relation is perceptible, and in these, the nature of the osteoporosis affecting the bone is doubtful. Glutin has been found in the cases in which the cartilage of such bones was examined for gelatin, and consequently the chemical constitution of the organic substance remained unchanged.

In a chemical point of view, *osteomalacia* has been more investigated than osteoporosis; but here we must distinguish between the osteomalacia of childhood, that is to say, rachitis, and the softening of the bones in adult life. Yet, notwithstanding the analyses of Marchand,* von Bibra,† Davy, and Ragsky, to which I

* Journ. f. prakt. Chem. Bd. 27, S. 92.

† Op. cit. p. 291.

may add my own,* we are still in ignorance of the pathological process and the morbid product of true rachitis. Our analyses are only so far accordant, that all agree in assuming that rachitis induces a considerable diminution of the mineral constituents of the bones, although it still remains to be decided whether this diminution may not be in part a relative one, depending merely upon an increase of cartilage. The assumption of many pathological anatomists, that the rachitic process is connected with true hypertrophy of the bone-cartilage, must at the present day be regarded as, to say the least, very improbable; for when rachitic bones, which have been only moderately macerated and deprived of their fat, are examined in thin sections under the microscope, the Haversian canals and *lacunæ* (bone-corpuscles) are not found to be filled with organic matter, but are either empty or dilated. If we calculate the analysis of an imperfectly macerated bone, containing all its fat (and the gelatinous substance effused into the medullary canals) for 100 parts, we shall indeed obtain an absolute excess for the organic constituents, and a relative deficiency for the inorganic matters; but these relations do not prove the existence of hypertrophy of the cartilage. Such a condition can only be microscopically and chemically shown in those rachitic bones which exhibit a tendency to healing through sclerosis; an absolute augmentation of the cartilage can be detected only in these cases, and not in the highest stage of the special rachitic process. Hypertrophy of the cartilage constitutes the basis, not of softening of the bones, but of osteosclerosis, more especially when it occurs after rachitis, or after osteoporosis. The nature of the cartilage generally remains altogether unchanged in rachitis; but Marchand and I have observed cases of highly developed rachitis, in which no glutin could be extracted from the bones, although after prolonged boiling, I obtained a slightly gelatinising substance which yielded some of the reactions of chondrin. An exact determination of the relations of the earthy constituents of rachitic bones is the more important from the light which they appear to throw on other processes, and on the nature of rachitis itself. The carbonate of lime appears from several analyses to diminish proportionally to the earthy phosphates, but other analyses (as for instance those made by Marchand and myself) yield a higher amount for the carbonate of lime than the normal proportion. Although the phosphate of lime is often much diminished, the rachitic process cannot be conditional upon the occurrence of free acid, as has been assumed

* Schmidt's Jahrb. der ges. Med. Bd. 38, S. 280.

from a single observation by Marchand. The assumption that carbonate of lime is removed from the bones, is controverted not merely by the result of analyses, but also by the indifferent behaviour of decidedly rachitic bones towards blue litmus. The ash of these bones occasionally yields more carbonate of lime than we calculate from the direct determination of the carbonic acid in the fresh bones (after being merely deprived of their fat); a portion of the lime must therefore have been combined with some organic acid, which, however, need not necessarily be lactic acid, since a fatty acid or some other substance may have been combined with this base. The frequent occurrence of free uric acid, lactic acid, and oxalate of lime, in the urine of rachitic children, cannot be regarded as affording evidence of the existence of a so-called lactic acid diathesis or dyscrasia; we shall indeed have occasion to show that the osteomalacia of adults presents more grounds for the establishment of such an hypothesis. Whether the basic phosphate of lime found in the bones of rachitic patients is converted into the $\frac{3}{8}$ basic salt is a question which must be decided by more exact and direct investigations than any hitherto made.

The *Craniotabes* (of Elsässer) is probably nothing but a form of rachitis which affects the occipital and parietal bones during the period of suckling, and we should, therefore, make no special reference to it, were it not for the purpose of drawing attention to the admirable investigations made by Schlossberger* on this subject, which may, indeed, serve as a model for all similar inquiries. He ascertained that the 63% of mineral substances, which he found to occur in the normal occipital bones of healthy children during the first year of their age, diminished to 51% in the simply attenuated parts of the bone, and to 40 or even to 28% in the thickened and spongy softened parts; he found that the carbonate of lime was present either in a normal quantity, or only slightly diminished, and that the cartilage was so far sound that it yielded ordinary glutin on boiling, whilst the fat, when compared with that in the rachitic bones of children of more advanced age, was not at all or very slightly increased.

The *osteomalacia of adults*, which undoubtedly depends upon osteoporosis accompanied with diminution of volume and a deposition of fluid fat in the dilated and newly formed cavities, would appear to be more referable than rachitis to the excessive formation of acid in the organism; but a thorough investigation of the nature of this remarkable disease and its products (such as that by

* Arch. f. phys. Heilk. Bd. 8, S. 69-87.

Schlossberger on craniotabes, to which we have already referred) is still wanting. Bostock,* Prösch,† Bogner,‡ myself,§ von Bibra, Ragsky, Gerster,|| C. Schmidt,¶ and Weber,** have submitted these bones to examination. The earthy constituents of the bones are more diminished here than in any of the other bone-diseases we have considered; but the physical examination shows that a large portion of the cartilage is also destroyed, whilst the almost brittle network of residual bony matter floats in thin fluid fat, which amounts in some cases to 20 or 30%. The osseous substance which is obtained from these bones occasionally yields glutin on boiling; but when the bones are very thoroughly affected by the disease, the organic matter yields no gelatinising substance like glutin or chondrin. I could not discover that the fat of these bones contained phosphorus, as Nasse†† found was the case with ordinary bones. C. Schmidt proved in the most unequivocal manner that free lactic acid was present in the fluid of the cylindrical bones. The fluid occurring in these bones exhibits very often, although not invariably, an acid reaction; and although the excessive quantity of fat may in some cases impede the action on litmus paper, I have known cases in which some of the bones of a patient affected with osteomalacia exhibited an acid reaction (as the femur and tibia), whilst others (as the ribs and pelvic bones) showed no trace of the presence of acid, even where there was a smaller accumulation of fat. We cannot, therefore, refer the resorption of the bones to the occurrence of free lactic or fatty acids, unless in direct opposition to well-attested facts. The occurrence of the lactic acid may perhaps be owing to the development of a chemical process in the broken-down fragments of the bones, which gives rise to the formation of an acid, as Gerster, Schmidt, and Weber observed in the case of perfectly disintegrated bones. The anatomical investigation, as well as the analysis of the individual morbid process, renders it more than probable that the occurrence of the fat in the bones does not exert a primary influence on their disintegration, but acts only in a secondary manner within the spongy parts. The mineral substances decrease very considerably

* Medico-Chirurgical Transactions, Vol. 4, p. 38.

† Comment. inaug. de osteom. adult. Heidelb. 1835.

‡ Valentin's Repert. 1842, S. 294.

§ Op. cit.

|| Arch. f. phys. Heilk. Bd. 7, S. 142-146.

¶ Ann. d. Ch. u. Pharm. Bd. 61, S. 281.

** Op. cit.

†† Journ. für prakt. Chemie. Bd. 27, S. 274.

when compared with the cartilage in this form of osteomalacia, as will be readily seen if we exclude the fat in the calculation of the analysis. It is remarkable that notwithstanding the acid reaction of the juice permeating the bone, carbonate, as well as phosphate of lime, is found in the macerated bones from which the fat has been removed, and that the former even appears to be less decreased than the latter. Weber is the only one who has investigated the composition of the phosphate of lime contained in these bones; he found, in addition to carbonate of lime, $\frac{3}{8}$ basic phosphate of lime, and believes that the phosphate of normal bone ($3\,CaO.\,PO_5$) is converted by means of the free acid into this less basic salt. If this interesting fact should be confirmed by future investigations, it must still appear very striking that so much carbonate of lime could be present in fresh bone, together with the free acid. The affections which we comprehend under the term osteomalacia may, therefore, possibly admit of being subdivided into two different processes. It will in like manner depend upon future and more carefully conducted investigations to determine whether, as we are induced from various reasons to believe, the arthritic process actually corresponds with that of osteomalacia.

Carious bones, the products of ulcerous ostitis, have been very carefully examined by Valentin* and von Bibra.† The ulceration so gradually destroys the bone, that the mineral constituents disappear to a greater extent even than the cartilage before the entire destruction of the osseous tissue, and that the cavities formed in the bones by caries become filled with fat in the same manner as in osteomalacia; hence we always find a larger quantity of organic matter in carious than in normal bones: the residual cartilage does not differ from the ordinary bone-cartilage, or at all events the decoction exhibits the usual reactions of glutin. It appears from most analyses that the carbonate of lime diminishes in direct proportion with the phosphate. Bibra endeavoured to ascertain whether the phosphate of lime exhibited any difference in the proportions of its proximate constituents in caries; he found $\frac{3}{8}$ basic phosphate of lime, but further investigation was required to determine this question decisively.

The chemical investigation of portions of *necrosed* bone has not yet led to any important results; nor can we wonder at this, when we consider the conditions under which separate bones, or portions of bones, are necrosed: that is to say, how they are

* Valentin's Repert. 1838.

† Pogg. Ann. Bd. 57, S. 356-372.

deprived of nutriment by the intervention of healthy parts. Our analyses yield, therefore, very nearly the same composition for necrosed as for healthy bones; the organic matter sometimes appears to be rather augmented, although it is occasionally slightly diminished; they commonly present the same characters as strongly macerated bones.

Fossil bones have also been made the subject of numerous investigations.* The locality from which they have been removed should always be considered in these inquiries, for to this we must obviously refer many of the modifications presented by their composition; thus, for instance, the mass in which they are embedded frequently exerts a chemical action upon them by decomposing or metamorphosing the organic matter or the phosphate of lime, whilst it also readily becomes infiltrated (especially its carbonate and sulphate of lime) into the bone-canals.

The quantity of organic matter contained in fossil bones varies very considerably; thus, for instance, in some cases the organic matter contained in them has been found to be scarcely diminished when compared with that of fresh bones, whilst on the other hand many of these bones exhibit no remaining trace of organic matter. We have already referred to the observation made by Bibra, that the cartilage of fossil bones is generally converted into a substance which at once yields glutin, after the mineral matters have been thoroughly removed. It seems *a priori* more than probable that the composition of the phosphate of lime might undergo a change in fossil bones; but still this salt has almost always been found to consist of 8 $CaO.3\ PO_5$, which is the same composition as that occurring in fresh bones. It is therefore very questionable whether the occurrence of small crystals of apatite, 3 $CaO.PO_5$, in fossil bones, or in bones which have lain for a long period of time in the earth (Girardin and Preisser†), can depend upon a metamorphosis of the chemical constitution, or (as seems less improbable) on an arrangement of the minute particles of phosphate of lime into crystals. Carbonate of lime generally occurs in far larger quantities in fossil than in recent bones, although this increase is frequently only relative, in consequence of the organic substance having disappeared from the bone; more commonly, however, this carbonate of lime is absolutely augmented either by infiltration from without, or in certain soils, from a portion of the phosphate of lime being decomposed by carbonic acid or carbonates. Mag-

* On the literature of this subject, see Vol. 1, p. 425.

† Ann. de Chim. et de Phys. 3 Sér. T. 9, p. 370-382.

nesia often occurs in larger quantities in the fossil remains of vertebrated animals than in the fresh bones of the present animal world. The greater abundance of fluoride of calcium which some of our best analysts have found to occur in fossil bones has excited considerable attention, more especially since Liebig* has shown that even the cranial bones excavated at Pompeii exhibit a larger proportion of fluoride of calcium than the bones of the present generation (see vol. i, p 424). On the other hand, Girardin and Preisser have found that the fluoride of calcium had greatly diminished in human bones which had lain long in the earth, and in some cases had even wholly disappeared. There is thus sufficient proof that it may increase as well as diminish in a perfectly normal manner in the bones, although this increase or decrease cannot always be referred to definite causal relations. Alumina, oxide of iron, and silica, are substances which are very frequently found in fossil bones, although we must undoubtedly regard their presence as due merely to infiltration.

We shall consider the bones and cartilages of the invertebrate animals in a subsequent portion of the work.

The *analysis of bones* is undoubtedly one of the simplest operations of zoochemical research, but so many different methods have been attempted that, notwithstanding the great number of analyses, we have arrived at no conclusive results; we see, for example, that the chemical composition of the phosphate of lime contained in the bones is still doubtful, even at the present time. Thus, too, a number of questions present themselves to our notice on entering upon the consideration of the constitution of pathological bones, which have either been wholly unanswered or very imperfectly solved by the analyses in our possession. A more exact knowledge of the specific gravity of the bones must have thrown considerable light upon their physiological and pathological conditions; but whilst in many cases, as for instance, in the examination of urine, the density of the fluid to be analysed is in general more or less accurately determined, the determination of this property has been almost entirely neglected in the case of the bones, excepting in the analyses made by Ragsky. Independently of the fact that the *density* is an important physical property, deserving special attention in the consideration of the numerous modifications to which the bones are subject in a healthy and morbid condition, we might expect, by a careful study of the subject, to ascertain the existence

* Die org. Ch. in Anwendg. auf Agric. u. Physiol. S. 140. [or English Translation, 1840, p. 156.]

of a definite law indicating a relation between the density and the proportions of organic and inorganic matters contained in the bone, which is obviously a point of the highest importance. As, however, the proportions both of water and of fat contained in the bone exert a great influence on its physical properties, and these must necessarily be most intimately connected with its specific gravity, it should be one of the first points in the investigation of this subject to institute a comparison between the specific gravities of different bones after being dried in the air, after the removal of their fat, and in a perfectly anhydrous condition. The determination of the absolute weight has been almost as much neglected as that of the specific gravity, in comparing together normal and diseased bones, although it is only from this determination and from a comparison with the specific gravity, that we can form a judgment of the metamorphosis of matter going on in the bone during any physiological or pathological process (and not from the proportional numbers of a single chemical analysis). Although we must presume that our readers are acquainted with the methods, cautions, and modes of correction required for the determination of the specific gravity, we would simply draw attention to the fact, that the pulverised bone (in all conditions under which it may be submitted to examination, whether it have been dried in the air, deprived of its fat, or have been wholly freed from water) should be kept for several hours in a vacuum after it has been well shaken and impregnated with distilled water, such a precaution being necessary for the thorough removal of all particles of air.

Few observers, with the exception of Nasse and Stark, have satisfactorily investigated the *quantity of water* contained in the bones. Nasse was indeed induced to believe, from his observations, that the water contained in bones exerted no influence on their hardness, but we cannot deny its influence in morbid bones on this and other physical properties. As bone is very hygroscopic, we ought to notice the state of the thermometer and hygrometer in comparing the quantity of water present in different bones which have been dried in air, before the pulverised bone is thoroughly deprived of its water in an oil or air-bath.

The determination of the quantity of fat contained in the bones is more uncertain than that of most of the other constituents. The fat, as we have already observed, is limited for the most part to the medulla of the bones, extending only slightly into the Haversian (or so-called medullary) canals. The fat which is not contained in the cavities and interstices of the bones, but adheres

to the true osseous tissue, is very inconsiderable in quantity, and is, at all events, only mechanically mixed with it; it should therefore, we think, be always merely compared with the quantity contained in other bones, and not be included in the percentage representation of the chemical analysis as a constituent of bone. The influence exerted by the fat of the true osseous tissue on its physical properties has not as yet been accurately ascertained. We have already spoken (in vol. i. p. 246) of the rules which should be observed in the determination of the fats.

In order to study the composition of the true osseous tissue (and this has been the object of most of the analyses hitherto made), the bones should in the first place be minutely pulverised, carefully washed with water, and then deprived of their fat by the action of ether; for the analysis can yield no clear representation of the composition of true bone until the fatty constituents, and the substances soluble in water, and derived from the blood and the bone-plasma, have been carefully removed. The presence of these substances not only increases the difficulty of the technical performance of the analysis, but the analysis itself naturally gives only a very imperfect result in relation to the osseous tissue in various physiological or pathological conditions.

It was formerly customary to calculate the quantity of *carbonate of lime* contained in bone by the quantity of lime in the fluid from which the phosphate of lime had been precipitated (according to Berzelius's method) by ammonia free from its carbonate; but this method has been shown by many analysts to be exceedingly uncertain. The quantity of carbonic acid in the bones should therefore always be determined by Fresenius's apparatus. It is very useful to compare the quantity of carbonic acid contained in the bones after they have been well washed and deprived of their fat, with that present in the ash. We usually find rather more carbonic acid in well-prepared ash than in fresh bone; this excess, which is slight in healthy bones, rises in some cases very considerably in morbid bones. This is indeed the only method which admits of our estimating how much lime is combined, not with carbonic acid, but with organic matter.

The method employed in preparing the bone-ash is not devoid of importance; for the determination of the earths, we must first wash the pulverized bone and thoroughly remove the fat by ether, and then after it is completely dried, submit it to the process of combustion. Erdmann's muffle affords the most rapid and complete means of incinerating bones; burning them in a platinum

crucible over Berzelius's lamp is a much less rapid method of proceeding; in either case it is advisable that the bone-ash should be moistened with carbonate of ammonia and again heated before it is weighed. There is almost always a more or less considerable quantity of caustic lime formed during incineration. When the above precaution is neglected, the ash is often found to yield less carbonic acid than the fresh bone, a result which may, however, depend upon other circumstances.

With regard to the individual determinations of the *phosphoric acid, magnesia, fluorine,* and traces of *sulphuric acid,* we presume that our readers are acquainted with the different methods employed in analytical chemistry; we would, however, especially recommend the mode of procedure devised by W. Heintz.*

We have only very unsatisfactory data for the determination of the *quantitative relations* existing between the bony skeleton and the whole weight of the animal organism in different classes of animals, and during different diseases; and in many cases we have no data of any kind.

At the age of 21 years, the weight of the skeleton is to that of the whole body in the ratio of 10·5 : 100 in man, and in that of 8·5 : 100 in woman (the weight of the body being about 125 or 130 lbs.)

The special consideration of the parts which stand in a close relation to the bones, such as the periosteum, the marrow, and the cartilaginous investments, does not fall within the limits of our inquiry, since they are organic parts composed of several simple tissues, and cannot, consequently, be made the subject of a rational chemical investigation.

Although numerous histological observations have been made on the development of the bones from cartilage, the subject has been very imperfectly considered in a chemical point of view. In reference to the development of individual bones, we scarcely know more at the present day than what was known long since, independently altogether of chemical investigations; namely, that the bone, as long as it continues in a state of cartilage, contains a substance yielding chondrin, which becomes converted into a body yielding glutin during the progress of ossification, when the earths are simultaneously deposited in the bone in large quantities. Boussingault made some interesting experiments on pigs in connection with the absorption of mineral substances during the development of the skeleton. It would appear from these obser-

* Monatsber. der Akad. der Wiss. z. Berlin. 1849, S. 50-53.

vations, that the skeleton of a pig increases on an average about 11·7 grammes in weight daily during the first eight months after birth ; that is to say, that about 6·2 grammes of cartilage are daily formed, and 5·5 grammes of earths (including 2·4 grammes of phosphoric acid) are taken up by the bones. At a subsequent period, as, for instance, till the eleventh month, the skeleton increases on an average about 6 grammes daily, that is to say, there are only about 2·6 grammes of earths (including 1·4 grammes of phosphoric acid) deposited daily in the bones.

The Teeth.

The teeth have commonly been considered, in a chemical point of view, as organs possessing very great analogy with the bones, and they have been regarded as purely mechanically acting parts, rich in mineral substances, and analogous to the products of inorganic nature—in short, to minerals; but this mode of investigating the subject cannot satisfy the requirements of the histologist or the physiologist. Independently of their mode of development, the structure of the teeth differs so entirely from that of the bones, and is moreover so complicated, that it would be wholly irrational to regard the teeth as formed of homogeneous simple tissues, and to submit them directly to chemical analysis.

When we analyse an entire tooth, we are guilty of the same error as the chemists of an earlier age who triturated complicated organisms in a mortar, and then attempted to analyse the chaotic mass. Even in a *chemical* investigation of the teeth, we should remember that every tooth consists of three morphologically different parts, namely, the dentine or tooth-substance, the enamel, and the cement.

The predominant part of the tooth, and that on which its form depends, is the dentine (*substantia tubulosa*), a fusiform or wedge-like body, provided with a club-shaped hollow extremity for the reception of the nerves and nutrient vessels. Histological investigation has shown that dentine is not a homogeneous body, but that it consists of a perfectly structureless* mass, resembling the matrix of bone, and perforated by a very large number of minute ramify-

[* In the previous edition Lehmann says "not perfectly structureless." According to Kölliker, the matrix of the dentine in the recent tooth is quite homogeneous. After the extraction of the calcareous salts from the dentine, it, however, exhibits a great tendency to break up into fibres.—G. E. D.]

ing canals. These canals have comparatively thick distinct walls, and proceed from the cavities, diverging towards the external surface of the dentine, in the vicinity of which they are still more minutely ramified. We do not observe bone-corpuscles, or other structures peculiar to bone, in the dentine; but in their place we have the *interglobular spaces* of Czermak,* which resemble the holes made by bullets. We must, therefore, take into account the contents of these tubes (probably the nutrient fluid of the tooth), and of the above-named cavities, in the chemical investigation of the fresh teeth. It is clearly shown by microscopico-mechanical examination, that here also the salts of lime are not deposited in the canals or cavities.

Hoppe † exposed to the prolonged action of boiling water thin sections of the molar teeth of the pig, the salts having been previously extracted with hydrochloric acid, and the cartilage of the cement having been removed with water. The external part swelled up, became transparent, and dissolved, with the exception of a few flakes; while, on the other hand, the interior became white and transparent, crumbled down, and was scarcely at all soluble. The solution only contained glutin. The undissolved residue, when examined under the microscope, presented the dentinal canals in a perfectly isolated state, and aggregations of dark globules with distinct nuclei: these globules perfectly corresponded with the above-mentioned interglobular spaces. Acetic acid dissolved neither the canals nor the globules. Hence, according to Hoppe, the canals, like the bone-corpuscles, possess independent walls which do not consist of a gelatigenous substance; Hoppe considers the globules to be cells.

Slight as is the resemblance between dentine and osseous tissue in a morphological point of view, there is still less similarity between the vitreous investment of the crown of the tooth (or the enamel) and bone. The enamel is a very hard and rather brittle compact mass, not permeated by canals or pores, and composed of fibres resembling 4 or 6-sided prisms, diverging from the crown of the tooth: whether these fibres (the so-called enamel prisms) are agglutinated together by a special intermediate substance, is not yet decided: a more accurate chemical investigation may probably enable us to determine this point.

According to Hoppe,‡ the enamel, after the extraction of its

* Zeitsch. f. wiss. Zool. Bd. 2, S. 295-322.

† Arch. f. pathol. Anat. Bd. 5, S. 170-188.

‡ Op. cit.

salts by means of hydrochloric acid, leaves structures which present the characters of epithelium; the remains of the prisms readily fall asunder, and do not dissolve on boiling, but break in pieces.

While the crown of the tooth is covered by enamel, the neck and root are invested with a layer of cement of varying thickness. The cement is a substance presenting the greatest resemblance to bone, and exhibiting the bone-corpuscles or bone-cavities with their prolongations; it differs, however, from dense bone in the absence of true Haversian canals.

Histologists have not hitherto succeeded in throwing any great amount of light on the chemical composition of these tissues composing the teeth, although Berzelius* and Lassaigne have certainly drawn attention to the essential differences existing in the composition of the dentine and the enamel, and von Bibra† has devoted much attention to the same subject. All that is known regarding the chemical constitution of the teeth and their individual histological parts, we owe almost entirely to these observers.

The *chemical composition of dentine* is very similar to that of bone; the organic matter consists of gelatigenous cartilage, whilst the mineral parts are precisely the same as those occurring in the bones. The quantitative ratio between the organic and inorganic matters in dentine is somewhat varying, approximating very closely in some cases to that occurring in the dense bones; but in the majority of the small number of cases recorded, the organic substance amounts to about 28%. A little fat is always found to be present with the cartilage. The mineral constituents of dentine are identical with those of the dense bones, and occur in nearly the same relative quantities. The quantity of carbonate of lime appears, however, to be more variable here than in the bones; from 3 to 8% of carbonate of lime have been found with from 65 to 67% of phosphate of lime. Berzelius demonstrated that fluoride of calcium and phosphate of magnesia are also present in the dentine.

The *enamel* differs in a chemical point of view from dentine, for no cartilage can be obtained from it, whilst the amount of the whole organic matter, which, after being treated with acids, appears like a membranous tissue, does not exceed 2·0 or at most 6·6% of the dried mass. From 81 to 88% of phosphate of lime, with about 7 or 8% of carbonate, are found in the enamel. We

* Lehrb. der Chem. Bd. 9, S. 553. (4 Aufl.)

† Op. cit. p. 276.

have already spoken of the abundance of fluoride of calcium present in the enamel. (See vol. i, p. 424.) The chemical investigations of this substance have left it undecided whether the phosphoric acid and lime enter into a different combination in the enamel and dentine from that occurring in the bones.

Although the *cement* of the teeth has been most imperfectly examined, yet von Bibra, Lassaigne, and Marchand concur in regarding this substance as more analogous in its composition to bone than dentine was found to be; it differs from the latter in containing a little more organic matter.

Lassaigne and von Bibra found on a average a rather larger quantity of mineral substances in the molars than in the incisors.

It would appear from observations made by Lassaigne, that the organic matter diminishes with age in the teeth as well as in the bones.

The comparative experiments of Lassaigne and von Bibra on the teeth of different animals have yielded very few results which would justify the establishment of general propositions; the last named of these observers could not even discover any definite difference in the composition of the teeth of carnivorous and herbivorous animals. Bibra's observations show that there is a striking relative excess of organic matter in the grinders of the elephant and the wild boar, and that the teeth of these pachydermata contain a very considerable quantity of phosphate of magnesia (as much, according to him, as from 6 to 12%).

Carious teeth do not very readily admit of chemical investigation; but it may be observed that, according to Marchand, the tendency of the teeth to this mode of destruction may be referred to their containing an excess of carbonate of lime.

The remarks already made concerning the *analysis* of the bones refer equally to that of the teeth; excepting only that it is more difficult to prepare the materials for examination in the latter case, more especially in exhibiting pure enamel or cement; the best method of obtaining the former of these substance is by heating the tooth to a few degrees above 100°, when one portion of the enamel becomes spontaneously detached, and the removal of adjacent pieces by mechanical means can be then readily effected. These detached portions require, however, still further cleaning to remove the tissue of the dentine which may be attached to them. In consequence of the difficulty of drying the enamel thoroughly when in masses, von Bibra's method should be adopted, which consists in pulverising the purified enamel, and then drying it.

Cartilage.

Cartilage belongs to that class of tissues which, although they appear to act for the most part mechanically, and to possess a small amount of vital activity, nevertheless exhibit a tolerably composite and very varied structure.

Histological investigations show that cartilage must be classed under at least two heads, depending upon structural differences: namely, true cartilage and fibro-cartilage.

Amongst the *true cartilages* of the human body we must include those of the ribs, the ensiform cartilage, the cartilages of the nose, of the larynx and trachea, and the cartilaginous masses investing the articular heads of bone. This true cartilage is so far identical in character in these parts of the organism, that it exhibits in all cases more or less numerous cavities occurring in a tolerably homogeneous mass, and containing one or more cells with a simple nucleus. This matrix is by no means perfectly amorphous; in most cases it is finely granulated, but frequently it is fibrous.

The *fibro-cartilage* composing the intervertebral ligaments, the *symphysis pubis*, the claviculo-scapular ligaments, the Eustachian tube, &c., contains, in addition to cells, a thoroughly fibrous matrix; these fibres are either parallel to, or intersect one another in various directions, present sharp dark outlines, and exhibit no trace of nuclei.

These differences, which the microscope reveals in cartilage, admit equally of recognition by means of chemical investigation. Müller's* observations, which were the earliest prosecuted in relation to this subject, have been followed in more recent times by those of Donders and Mulder.†

When we examine this tolerably homogeneous matrix of true cartilage in a chemical point of view, we find, on carefully treating the triturated cartilage with boiling water, that it is this substance, and not the cartilage-cells, which yields the chondrin described in vol. i, p. 398. Thus, for instance, if we boil the cartilage of the ribs from 12 to 48 hours in the open air (Mulder), or from three quarters of an hour to an hour in a Papin's digester (Hoppe‡), the matrix will be dissolved, leaving only the other morphological

* Pogg. Ann. Bd. 38, S. 295.

† Versuch einer phys. Chem. S. 658 [or English Translation, pp. 545-559.]

‡ De cartilaginum structura et chondrino, diss. inaug. Berol. 1850.

elements of the cartilaginous tissue, namely, the cartilage-cells and their nuclei, which remain undissolved, together with vessels and the coagulated protein-bodies of the blood-plasma. Before the solution of chondrin is perfectly gelatinised, a small deposit is generally formed, and in this these morphological elements may be readily and distinctly recognised by the microscope. But there is a slight opalescence observable even in the clearest solution of chondrin, which is owing to the suspension of these cells and their fragments. The chondrin which has been examined by chemists, must therefore always contain a larger or smaller quantity of morphological elements, which cannot be perfectly removed, even by Hoppe's very admirable mode of procedure. We cannot, therefore, regard the elementary analyses of chondrin as more trustworthy than those of cartilage itself, since we have to deal in both cases with a mixture of obviously different bodies, and not with a simple chemical combination. It is alike remarkable and worthy of regret that the elementary analyses of these substances should have yielded such identical results; several of our most distinguished and skilful analysts having found that the composition of cartilage, which abounds in cells, and of chondrin, which contains only few cells, although not entirely devoid of them, is almost entirely identical. Setting aside the cells altogether, there would appear grounds for concluding that the conversion of the cartilage into chondrin depends only upon a deposition of atoms, and not upon chemical decomposition due to the assimilation or elimination of certain elements.

According to the micro-chemical investigations of Donders and Mulder, the matrix of cartilage has far less power of resisting the stronger chemical reagents, such as concentrated sulphuric acid or a strong solution of potash, than the cells contained within it. Its behaviour towards concentrated sulphuric acid shows, however, that even this matrix is not a perfectly pure chemical body. Thus, for instance, on the application of concentrated, and afterwards of diluted sulphuric acid, the granules of the granulated cartilage are less rapidly dissolved than the matrix itself, whilst the fibres of the fibrous mass yield still later to this action. It appears, therefore, probable that the matrix may contain three different, although very nearly allied, substances. The question whether the difference existing in these three substances depends upon a different aggregation of the very minute mechanical particles, or whether it is of a chemical nature, is one which even the latest observations, made on the chondrin obtained from the decoction of the matrix, have

failed in deciding. The inquiry is rendered the more difficult by the circumstance, that the chondrin itself becomes partially changed during the process taken to obtain it; chondrin being converted, like glutin, by boiling into a substance which does not gelatinise, and is soluble in cold water.

The products of the decomposition of chondrin have also failed in affording us any important results; we merely know from Hoppe's observations, that chondrin, when decomposed by concentrated sulphuric acid, yields (in addition to extractive matters) leucine only, and no glycine, but when treated with a concentrated solution of potash, glycine only, and no leucine, besides extractive matters.

The fibrous matrix of fibro-cartilage must have a totally different composition from that of true cartilage, as we see from the micro-chemical investigations of Donders and Mulder. After exposing cartilage of this kind (as, for instance, one of the intervertebral bodies) for a moderate time to the action of a concentrated solution of potash, or of sulphuric acid, the fibrous character of the matrix, when observed under the microscope, is found gradually to disappear, but these agents fail equally with concentrated acetic acid in actually dissolving it; for a close examination shows that the individual fibres merely swell and assume a gelatinous appearance, and consequently become less perceptible to the eye. Donders further observed that, in addition to the cartilage-cells, there were fibres situated between these gelatinous bundles, which remained almost wholly unchanged in the sulphuric acid, and bore some resemblance to nuclear fibres, and besides these there were some fibres of connective tissue. The fibro-cartilages dissolve for the most part on boiling, and leave only a deposit of granular nuclei and a few cells. The gelatinising fluid obtained from these cartilages exhibits nearly the same reactions as the chondrin extracted from the intercellular substance of true cartilage. According to Donders, this solution yields only a slight precipitate with tannic acid, but on the addition of alum yields, like chondrin, a compact deposit, which, however, does not disappear in an excess of the solution. Bichloride of platinum produces a considerable precipitate, which is insoluble in an excess of the test.

The semilunar cartilages of the knee-joint have commonly been reckoned amongst the fibro-cartilages, but J. Müller showed long since, (in the case of the sheep,) that they yield no chondrin, but glutin only, on boiling. Donders, Kölliker, and other histologists, agree in considering that these cartilages, like the inter-

articular cartilages of the lower jaw, of the sterno-clavicular articulation, and of the wrist-joint, consist of true but very solid fibrous connective tissue, inclosing true cartilage cells, in addition to a few nuclear fibres. We cannot wonder, therefore, that (as connective tissue always yields glutin) these cartilages should, on boiling, yield ordinary glutin or bone-gelatin, notwithstanding the presence of cartilage-cells.

Donders distinguishes a third kind of fibro-cartilage, which he terms *elastic;* to this class belong the cartilages of the larynx, and the external ear, and the cartilage investing the condyle of the lower jaw. These structures consist of a dense tissue of fine elastic fibres, in which isolated cells are inclosed. These fibres are not altered by the action of a concentrated solution of potash, but the cells disappear after four or five hours; even after the application of sulphuric acid, the elastic fibres remain almost unchanged, while the cells are found to have disappeared after six or eight hours' action, and on the repeated addition of water.

On boiling these cartilages in water, Donders obtained only a little chondrin, and as elastic tissue generally is not gelatinous, he referred this chondrin to the metamorphosis of the cells, the more especially because he found that after these cartilages had been boiled for five or more hours no cells could be any longer discovered by the microscope. Hoppe, on the other hand, considers that during the process of boiling, the cartilage-cells in part escape from the elastic tissue, while the residual tissue so completely surrounds the cells that are retained, that they can only be recognised by the aid of a compressor. He is further of opinion that, possibly, Donders might not have sought in the fluid for unchanged cartilage-cells, and that he could not see them in the contracted tissue without using a compressor.

The present does not appear a fitting place to enter into a consideration of the different forms and groupings of the *cartilage-cells or cavities,* of their scattered occurrence or arrangement in rows, of the endogenous formations of parent and secondary cells of the first and second generations, &c.; although all these relations could obviously not exist without simultaneous differences in the chemical substrata. Our chemical knowledge is, however, still too defective to admit of our hazarding any conjecture in reference to the methods by means of which we may hope to ascertain the controlling chemical relations.

Mulder and Donders saw the morphological elements of true cartilage disappear into very fine granules when exposed under

the microscope to the action of a solution of potash, sulphuric acid and water; the granular or slightly fibrous intercellular substance first disappeared, next the margin or investing membrane of the original parent-cells (which also disappears after prolonged exposure to the action of acetic acid), then the membranes of the cells, and finally their nuclei. If from this it would seem a probable conclusion that the cell-walls and the nuclei did not essentially differ in their chemical constituents from the intercellular substance, the more especially as by continuous boiling with water the cells appear to be expelled and converted into chondrin, yet Mulder and Donders were led, from the relations of elastic fibro-cartilage, to the view that the morphological elements of cartilage closely resemble, in a chemical point of view, the intercellular substance, and that the observed differences are only dependent on a varying degree of cohesion of the deposited materials. The elastic fibro-cartilages, for instance, yield chondrin on boiling, while, with the exception of the cartilage-cells, they appear to contain no chondrin-yielding substance; while, on the other hand, the semilunar cartilages of the knee, notwithstanding their containing an abundance of cartilage-cells, yield only glutin, and not a trace of chondrin. It was this last-named circumstance that induced Hoppe* to take up the rigid investigation of fibro-cartilage and its relations, and he came to the conclusion that the cartilage-corpuscles are imbedded in a chondrin-yielding substance within the elastic tissue. He found, namely, that after elastic fibro-cartilage had been boiled for three hours, a certain amount of chondrin was formed, but that the cartilage-cells (for the most part perfectly unaffected) might be observed in the fluid as well as in the residual, strongly contracted elastic tissue. (The compressor was requisite to see them in the latter.) Hence Hoppe concluded that cartilage-cells cannot consist of gelatigenous substance, and was led to the axiom that cell-membranes and cell-contents never consist of such a substance, and further, that a cell-membrane can never be metamorphosed into gelatigenous tissue. Donders has, moreover, essentially modified his former view regarding the chemical constitution of the walls of the cartilage-cells, and both these experimentalists may be regarded as perfectly coinciding in these general statements and results. (See "Elastic Tissue.")

Mulder first proved that chondrin contains a small quantity of *sulphur*; but the amount of this substance in the tissue of true cartilage, and whether the sulphur exists in all, or only in some of

* Arch. f. pathol. Anat. Bd. 5, S. 170-188.

the morphological constituents of the cartilage, are questions still to be answered.

Fat has been found in the cartilages to the amount of from 2% to 5% of the dry substance; it occurs principally in the cells, but is also found in solitary globules and in the intercellular substance of true cartilage. Small fat-globules may be discovered in almost all cartilage-cells in addition to the simple or multiple nucleus, and occasionally the nucleus is rendered perfectly invisible by being completely enveloped in fat. No very essential difference has been found to exist between this fat and the fat of other organs.

The *amount of water* present in the cartilage, and which must obviously exert considerable influence on its physical properties, varies in different cartilages, fluctuating between 54% and 70%. No definite series of experiments, conducted on a given system, have been made in relation to the quantity of water contained in different cartilages, or as regards the specific gravity of these tissues.

From 3% to 6% of *mineral substances* have been found in the cartilages, but the experiment was limited to the cartilages of the ribs, and even these have not been examined with sufficient accuracy. Phosphates of lime and of magnesia, chloride of sodium, carbonate of soda, and (what is more remarkable) a large quantity of sulphates, were found; but it can hardly be doubted that the latter are in part due to the sulphur of the organic substance of the cartilage. The occurrence of alkaline carbonates indicates, as Berzelius* has shown, that the cartilaginous substance must be partly combined chemically with lime or soda; but whilst Fromherz and Gugert found upwards of 18% of carbonate of lime in the ash of cartilage, von Bibra† found at most only traces of alkaline carbonates in the costal cartilages of the human subject at different ages, as well as in those of animals. The very variable quantity of chloride of sodium found in the ash of cartilage (from 1% to 8%) would seem to indicate that it does not exist in chemical combination in the cartilage, but that it originates in the special juice which permeates that tissue, and which, unfortunately, has not yet been investigated.

The methods to be adopted in *the analysis of cartilaginous tissue* are sufficiently obvious from the remarks in the preceding pages.

[Much information on bone, the teeth, and cartilage, will be

* Lehrb. d. Chem. Bd. 9, S. 563.

† Op. cit., pp. 412-417.

found in Schlossberger's "First Attempt at a General and Comparative Animal Chemistry,"* now in the course of publication. —G. E. D.]

Connective Tissue.

The term *connective* or *areolar* is applied to a tissue which is chemically allied to cartilage, although of a simpler character, and is understood by histologists to comprise not merely that porous, soft, cellular tissue, characterised by the readiness with which it may be filled with air, which connects together the organs and various tissues of the animal organism, and was formerly termed *cellular tissue*, but also those morphological elements which constitute the solid basis or the main constituent of no inconsiderable number of animal membranes and ligaments. This tissue, uniting the organs with one another, which forms a network of variously sized meshes, composed of long slender fibres, for the most part combined in bundles, has been named *amorphous* connective tissue, but it very gradually passes into the *formed*† variety; the serous membranes and muscular fasciæ contain a dense network of rather large meshes; when the bundles of fibres follow a more definite direction, and approximate more closely to one another, forming dense striated masses, tendons and ligaments, will be the tissues developed from them. The connective tissue may also, to a certain extent, impart their form to the bursæ mucosæ, to the matrix of the mucous membranes, to some of the above-mentioned inter-articular cartilages, to the sub-mucous areolar tissue of the intestine (the *Tunica nervea*), to the dartos, to the longitudinal and annular fibrous coats of the veins, &c.

Unfortunately, however, a careful microscopico-mechanical examination shows that the tissue we are investigating is not a simple one. All its parts contain, without exception, heterogeneous matters, differing both mechanically and chemically from the substance of the true connective tissue; and hence chemists have hitherto been unable to make an analysis of this tissue in a per-

* Erster Versuch einer allgemeinen und vergleichenden Thierchemie. Von Julius Eugen Schlossberger. Erste Lieferung. Stuttgart, 1854.

† [The terms *amorphous* and *formed* connective tissue were introduced by Henle; they correspond to the *loose* and *solid* connective tissues of Kölliker.—G. E. D.]

fectly unmixed condition. In addition to vessels, nerves, fat-cells, and similar structures, the connective tissue constantly exhibits *elastic fibres* (*nuclear fibres*), and very frequently also *smooth muscular fibres.* As these intermixed parts do not admit of being mechanically separated from true connective tissue, such tissues only have been selected for chemical analysis as present the fewest of these morphological elements. On this account the tendons, for instance, have been chosen for analysis. But when so accurate an analyst as J. Scherer* has found that the chemical elements are in the same numerical relations in tendon, notwithstanding this admixture, as in the glutin produced from connective tissue, we cannot wholly reject the assumption that the connective tissue possesses the same elementary composition as glutin. Much weight cannot, however, be attached to conclusions drawn from the best elementary analyses of these substances with high atomic weights; for even the fact that the tendinous tissue intersected with elastic fibres was found to present the same ultimate composition as the glutin produced only from the fibres of connective tissue in the tendons, sufficiently proves that our analytical methods are not very sensitive in detecting slight admixtures of even very different substances. We should, however, be guilty of rashness, if we regarded it as an established fact, that the connective tissue is isomeric with glutin; for the constitution of the latter has not been determined with certainty.

On placing connective tissue in boiling water, it usually at first contracts, but soon swells up, assumes a gelatinous form, and dissolves after prolonged boiling (the length of time depending upon the density of the tissue, or the minuteness of its previous division). It contracts also in a slight degree, and thus loses the tendency to putrefaction, when treated with bichloride of mercury, alum, basic sulphate of iron, and tannic acid. If the connective tissue is treated for a prolonged time with dilute acids or alkalies at the boiling point, it is found to be much more rapidly metamorphosed into glutin than when it is boiled in mere water.

The connective tissue swells in concentrated acetic acid and becomes transparent, or at all events this is the case with the tendons, ligaments, &c., which are chiefly formed of this tissue; but this gelatinous mass is only thoroughly dissolved on the addition of water and the application of heat, and neither red nor yellow prussiate of potash produces any precipitate from this acetic-acid solution. The true fibres of the connective tissue are found by micro-chemical in-

* Ann. d. Ch. u. Pharm. Bd. 40, S. 1-45.

vestigation to swell on the addition of dilute acetic acid, and to become transparent, till they finally altogether disappear; but they are not actually dissolved even after many hours' exposure to this action, for on washing with pure water, or on neutralising the acid with ammonia, they may be rendered perfectly visible in their original form. As most of the other textural elements which are intermixed with the connective tissue are not similarly affected and rendered invisible by acetic acid, they are brought more distinctly in view by its application; and hence this agent becomes a valuable aid to the histologist in his study of the tissues.

The fibres of connective tissue also swell and assume a gelatinous form in alkalies, but after the prolonged action of the alkali they cannot be again brought to view by the addition of water, being completely dissolved.

We thus close our remarks on these three groups of tissues, which were all indicated as gelatigenous, even by the older histologists, and in which the most recent investigations have recognized a very surprising analogy. The labours of Virchow,* Donders,† and Kölliker,‡ have thrown much light upon this subject. Donders and Virchow especially coincide in this point, that the gelatigenous intercellular substance of these tissues does not originate from cells, but is directly separated from a plastic fluid, while the other elements in these cases (as for instance, in bones, the bone-corpuscles with their prolongations; in cartilage, the cartilage-cells; and in connective tissue the nuclear or elastic fibres with their nuclei) are primarily formed from cells. Kölliker is also convinced that the nuclear fibres are undoubtedly not formed from the nuclei of the cells of embryonic connective tissue, but from the cell-walls, but he denies that the fibrillæ of connective tissue are a direct deposition from the cytoblastema.

We must not here overlook the fact, which is remarkable in a chemical point of view, that the embryonic connective tissue, according to Scherer, contains no gelatin, but consists, in addition to fusiform cells, of a peculiar intercellular substance, which on digestion with water yields not only albumen, but a gelatinous or mucous substance. Virchow has proposed the term "mucous tissue" for this class of structures, of which the gelatinous substance of Wharton (in the umbilical cord) affords the best example.

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 150 u. 314.

† Zeitsch. f. wiss. Zool. Bd. 3, S. 348.

‡ Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 3, S. 1.

Elastic Tissue.

The elementary fibres of this tissue are somewhat extensively distributed in the animal organism, although they seldom occur in sufficiently large quantities to form special organs; they occur, for instance, in the yellow elastic ligaments (the ligamenta flava of the vertebral column, the inferior vocal cords, the ligamentum nuchæ of mammals, the elastic ligaments of the claws of animals of the Felidæ, and the hinge-ligament of bivalves). We meet with larger groups of elastic fibres connected into membrane-like sheaths in the fascia lata, and in the middle coat of the arteries and veins. Smaller accumulations of elastic fibres also occur in many other parts, as for instance, in the corium, and under the mucous membrane, more especially in the pharynx, the pylorus, the cæcum, &c. We need only observe here that the elementary fibres of this kind are met with under different forms of grouping, either in wide-meshed or very intricately formed nets having hook-like indentations; as fenestrated membranes exhibiting tolerably large intervals, and resembling an anastomising vascular network; or lastly, only as bundles or fibres twining around other tissues in a spiral manner. It is at the present day assumed by most histologists, that these true elastic fibres, which occur in the form of flat, rather broad, somewhat brittle, and much ramifying bands, are perfectly identical with those far narrower, spirally coiled *nuclear fibres*, which are often studded with nuclei, and are invariably present in connective tissue; and they have arrived at this conclusion, partly from watching the development of these tissues, and partly because the slightest transition from one form to the other admits of recognition; moreover, the chemical reactions of the two forms do not indicate any difference between them.

The elastic fibres never occur independently of other histological elements, however much they may predominate; most commonly they are found intermixed with the fibres of connective tissue, very frequently also with smooth muscular fibres (Kölliker's fibre-cells),* as in the middle coat of the arteries. Close to the fenestrated coat, the elastic fibres, intermingling in part with nuclear fibres, merge into the so-called contractile tissue, which is principally formed of these smooth fibres, to which they undoubtedly owe the property of contracting under the action of cold (Schwann†) or magnetic

* Zeitschr. f. wiss. Zool. Bd. 1, S. 78-82.

† Müller's Handb. der Physiologie. Bd. 1, S. 170, u. Bd. 2, S. 29 [or English Translation, Vol. 1, 2nd edition, p. 218, and Vol. 2, p. 876.]

electricity (E. H. and E. Weber*). The elastic fibres themselves are wholly deficient in animal contractility, and are only distinguished for their extraordinary elasticity, a property which is not destroyed by spirit, or by boiling (J. Müller).

The *chemical* investigations of elastic tissue which have been hitherto made, have unfortunately not led us to any clear knowledge of its constitution and general chemical relations. J. Müller† and Eulenberg ‡ obtained by the prolonged boiling of elastic tissues, a non-gelatinising fluid, which yielded some reactions similar to those afforded by long-boiled chondrin. Mulder and Donders§ failed, on the other hand, in obtaining any gelatinous substance, after forty hours' boiling, from well-purified elastic tissue, which had been freed from all admixture of connective tissue and fibre-cells, by means of acetic acid and a solution of potash; and they also found on making a micro-chemical examination, that the fibres were entirely unchanged.

M. S. Schultze|| has arrived at the conclusion, that the purified elastic fibre of the arterial coats is but slightly, or not at all changed, even after it has been boiled for sixty hours with water; whilst on the other hand, it becomes converted into a brownish non-gelatinising fluid, which has an odour of gelatin, after 30 hours' boiling at the temperature of 160° in a Papin's digester. This fluid was precipitated by tannic, picric, and kinic acids, tincture of iodine, and corrosive sublimate, but not by other reagents which commonly precipitate chondrin. We cannot conclude with Schultze, from these reactions, that the elastic tissue yields gelatin; for it would, in our opinion, be attaching too wide a significance to the idea of gelatin, were we to apply this name to substances which do not gelatinise, and merely yield precipitates with tannic acid and similar substances, which precipitate a great number of organic matters, and in other respect, exhibit only negative properties. In that case, we should be compelled to include Mulder's tritoxide of protein under the head of gelatin, and to denominate as gelatigenous numerous other matters, such even as albumen, since when boiled in water under high pressure and at a high temperature, they yield substances which are soluble in water, although they do not gelatinise.

* Berichte der k. sächs. Gesellsch. d. Wiss. 1849, S. 91.

† Pogg. Ann. Bd. 28, S. 311-313.

‡ De tela elastica; diss. inaug. Berol. 1836.

§ Mulder's Vers. einer phys. Chem., S. 594 [or English Translation, p. 543].

|| Ann. der Ch. u. Pharm. Bd. 71, S. 277-295.

According to the investigations of Donders and Mulder, elastic fibre is entirely insoluble in cold concentrated *acetic acid.* It is only after continuous boiling for some days in this acid that it gradually dissolves.

When heated with moderately diluted *hydrochloric acid,* it dissolves with a brown colour; the dissolved substance is soluble in water and in alcohol.

Xanthoproteic acid is formed by the action of *nitric acid.*

According to Zollikofer,* when pure elastic fibre is digested in *sulphuric acid,* diluted with $1\frac{1}{2}$ times its weight of water, it yields leucine only, and no glycine.

[We may here remark, that Zollikofer recommends the following as the best method of preparing leucine. Take elastic tissue, (for instance, the ligamentum nuchæ of the ox,) purify it by extraction with boiling acetic acid and with water, and afterwards boil it for forty-eight hours with sulphuric acid of the above-mentioned strength, then neutralize with milk of lime, boil the pulpy mass that is now formed, and filter. During the evaporation of the filtered fluid on the sand-bath, the lime-salts that become deposited must be as far as possible removed. On further evaporation in the water-bath, the fluid readily yields crystals of leucine. No glycine (as is remarked above) is formed, and the leucine may be purified without animal charcoal by mere recrystallization in spirit and alcohol.—G. E. D.]

Elastic tissue remains unchanged for a long time, at an ordinary temperature, in a moderately concentrated *solution of potash,* and it is only after it has been heated for some days that it becomes converted into a gelatinous mass.

Pure elastic fibre cannot be obtained by mechanical means, but must be procured, as we have already observed, by removing the fibrillæ of cellular tissue and the fibre-cells by boiling with acetic acid, and then adding a dilute solution of potash.

Tilanus found in the elastic substance of the ligamentum nuchæ, after it had been purified in the above-described manner, 55·75% of carbon, 7·41% of hydrogen, and 17·74% of nitrogen. We do not think that any reliable formula can be obtained from this analysis, even by the help of the analysis of the chlorine-compound.

Donders† has recently come to the view, that all *cell-membranes* consist of a substance identical with, or at all events, very

* Ann. der Ch. u. Pharm. Bd. 82, S. 168-180.

† Zeitsch. f. wiss. Zool. Bd. 3, S. 348-358, and Bd. 4, S. 242-251.

similar to elastic tissue. This opinion is specially based on histological grounds, and rests, on the one hand, on the development of elastic tissue and especially of nuclear fibres from the walls of cells, and on the other hand, on the circumstance that certain membranes and textural elements, which in their physical and chemical properties closely approximate to elastic tissue (as for instance, the sheaths of the nerves), may be found to be formed from cell-membranes. According to Donders, the walls of all true cells, whether occurring in the neurolemma, the capsule of the lens, &c., have the following physical and chemical properties in common with one another and with the elastic tissue obtained from them. The physical properties are their structureless, glossy character, their transparency, elasticity, strong refractive power, and a specific gravity higher than that of water. The chemical properties are their insolubility in water, alcohol, and ether (all the physical properties remaining unaffected by the application of these reagents)—their insolubility in acetic and other vegetable acids—their difficult solubility in dilute sulphuric, hydrochloric, and nitric acids—their insolubility in ammonia, and their slight solubility even in concentrated solutions of soda and potash—their swelling in acids and alkalies, and their alkaline solutions gelatinising—their difficult solubility in boiling water, and the absence of gelatinisation in the solution. The animal cellulose is rendered yellow by nitric acid, then after the addition of ammonia, orange; the colour is scarcely affected by hydrochloric acid, or by a mixture of sugar and sulphuric acid; it is turned red on the application of Millon's test. Acetic acid throws down from the alkaline solution a substance which is insoluble in an excess of the reagent, and possesses the main characters of animal cellulose; it does not readily become decomposed, even in morbid processes, if we except fatty degeneration.

However important such generalizations of the facts in our possession may be for histology—however such general views may throw light on the further progress of this science, and may open out future paths of inquiry, it would be by no means expedient, in the present state of our knowledge, to regard all cell-membranes as perfectly identical with the substance of elastic tissue; for independently of the circumstance that the above-mentioned properties are not found in every cell-membrane and in every elastic membrane, we know how differently reagents often act on cells and tissues, according to their age or the state of their development. Further, it can scarcely be questioned that the walls of very young cells, as for instance, blood-corpuscles, pus-corpuscles, the deepest epi-

dermic and epithelial cells, and the cells of the glandular follicles (Kölliker), are composed of a protein-body, that is to say, a substance far more nearly allied to albumen and fibrin than to the matrix of elastic tissue, seeing that they are readily soluble in acetic acid, and in very dilute alkalies.

Horny Tissue.

In former times the tissues belonging to this class were regarded as amongst the simplest in the animal organism, and considered merely as different forms of one and the same matrix, which certain chemists were ready enough to discover, and to designate by the term *Keratin.* The zealous labours of recent histologists have, however, shown us that even these apparently homogeneous tissues have a complicated, and in many respects, a variable structure. There exists the same correspondence between the structure of the epidermis, the nails (claws and hoofs), the horns, and whalebone, as that which we observe in the chemical constitution of these tissues, all of which are so far analogous to one another that they proceed from cells or nucleated vesicles, which are not morphologically developed like the cells of other organs, but to a certain extent dry up, and are only agglutinated together by an intercellular substance, which often does not very readily admit of detection. They also exhibit great resemblance in a chemical point of view, for when compared with other tissues they all contain a large quantity of sulphur in combination with a substance, or with atomic groups, whose origin from, or affinity with the so-called protein-bodies cannot be denied when we consider their behaviour towards certain reagents, and their per-centage composition. Although we are still far removed from a correct knowledge of the chemical constitution of these tissues, or rather of their elements, chemistry has, nevertheless, very largely contributed to place the question of the histological conformation of these tissues on a level with the present state of science; in confirmation of which we need only indicate the admirable labours of Donders* and Mulder, of Paulsen†, Kölliker,‡ and several other observers.

* Holländische Beiträge. Bd. 1, S. 39 u. 126, and Mulder's Vers. ein. physiol. Chem. S. 542-579 [or English Translation, pp. 493-530].

† Observationes mikrochemicæ ; diss. inaug. Dorpati Liv. 1848.

‡ Mikrosk. Anat. Bd. 2, S. 58-62, u. 85-88.

The questions to which the present condition of histological inquiry leads the chemist in his examination of the horny tissues, are briefly these:—Is there a substance which holds together the cells of these tissues, agglutinating them to a certain extent, and, if so, what are the chemical properties and the composition of this substance? What is the chemical character of the morphological constituents of these dried cells or vesicles of the horny tissue? What is the nature of the cell-membrane, and of the nuclei which exist in almost all of the cells, and finally, of what do the generally dried contents of these cells consist? Are the morphological elements identical in different kinds of horny tissue, or do they often differ essentially from one another, as various reactions would seem to indicate? What is the constitution of these morphological elements in the newly forming or just formed cells in the vicinity of the *rete mucosum* of the skin or the mucous layer of the nails? What metamorphoses do analogous elements undergo during the gradual drying and the alterations in form of the originally filled spherical or oval cells?

It unfortunately happens that the chemical investigations hitherto instituted on this subject have contributed rather to the suggesting than to the answering of these questions; for although chemical reagents have enabled us duly to examine the morphological elements of the horny tissue, chemistry is still wholly incompetent to indicate the position which, from its form, each structure ought to occupy in the series of organic atomic groups. We should consider it a great step in advance, if we knew how to isolate any one of the morphological constituents of the horny tissue, in the same manner as we can isolate elastic fibre by chemical means from the yellow ligaments or the middle coat of the arteries. The different horny tissues have hitherto been regarded by chemists simply as homogeneous bodies, and analysed as such, after they had been freed by indifferent solvents from fat, salts, and the so-called extractive matters. Although these kinds of analysis have most frequently been conducted under Mulder's superintendence, no one is more thoroughly convinced than Mulder himself of their insufficiency in respect both to the histological and chemical knowledge of these tissues.

We abstain from entering more minutely into the consideration of the internal structure of the different horny tissues, as the observations already made on this subject will sufficiently explain the state of our chemical knowledge of these structures. The micro-chemical reagents to which we are now about to refer, afford, as we

have already observed, a closer insight into the histological than the chemical constituents of the horny tissues.

The horny tissues become gradually loosened when treated with cold or warm *water*. The epidermis is rendered so soft after prolonged soaking, as to admit of being easily broken down, and separated into individual cells, or smaller accumulations of them. The cells themselves are rendered more distinct; the extremely thin, irregularly formed epidermic plates appear somewhat swollen and faintly granulated. The nucleus, if one be present, becomes more distinct. The cylindrical or round cells of the *rete mucosum*, which contain a nucleus, and resemble vesicles expanded with fluid contents, are but slightly altered by the action of water.

The nails are on the whole very similar to the epidermis; however they only swell in water and become softer, without admitting of being triturated.

Horns and hoofs soften in water, especially on the application of heat, and then commonly develope a little sulphuretted hydrogen. The cellular structure cannot easily be recognised under the microscope, even after the tissue has lain for a long period in water; scarcely anything beyond fibres, which often appear to be torn, can be detected.

Water produces no visible alteration on whalebone or tortoiseshell, whether it be applied hot or cold, and however long it may be suffered to act upon either.

The best reagents for exhibiting the cellular structure of all these tissues are highly concentrated solutions of the *caustic alkalies;* in many cases *caustic soda*, as recommended by Kölliker, is preferable to *caustic potash*. A dilute solution of potash or soda, especially on the application of heat, acts, however, more rapidly upon the epidermis, and exhibits its cellular structure far better than the concentrated solutions. The concentrated solutions render the epidermic plates roundish, pale, and smaller; and it is only after a prolonged action that they swell, and distinctly exhibit their cellular form. Dilute alkalies convert the epidermic plates, in a short time, into oval or spherical clear vesicles, without a nucleus or granular contents. The cells of the *rete mucosum* show still more distinctly that the nuclei of the epidermic cells are sooner and more rapidly dissolved than their cell-membranes; for if the epidermic cells are exposed to the prolonged action of hot solutions of caustic alkalies, the cell-walls become dissolved, so that there only remains a small gritty and partially granular mass.

A solution of potash acts upon the substance of the nails in

the same manner as upon the epidermis, converting it into a mass of colourless non-nucleated vesicles; but, according to Kölliker, a dilute solution of caustic soda brings into view the most beautiful polygonal or oval cells, with distinct nuclei.

The fibrous structure of cows' horn disappears under the prolonged action of a concentrated solution of potash, but no cells (especially nucleated ones) become distinctly visible until water has been poured over the object. After repeated neutralisation with sulphuric, or even acetic acid, the cells generally appear in the form of oval or spherical vesicles without contents; the nuclei have consequently disappeared.

Whalebone consists, according to Mulder and Donders, who have subjected it to a very exact histo-chemical examination, of thin lamellæ, which lie parallel to the outer surface, and to the tubular system which resembles the medullary canals. Each of the lamellæ consists of a number of compressed cells, which are brought into view by the action of water after they have been treated with concentrated caustic potash. In this case, also, the cell-wall resists the action of the reagents for a much longer period than the nucleus and the other contents.

The same observers were also the first who accurately examined tortoise-shell; they found that this tissue also breaks up into polygonal and oval cells on the application of caustic alkalies, although a much more prolonged action of the potash is necessary here than in the case of the above-described horny tissues. The cells are not very readily isolated, and it is only on the addition of water that they appear individually; they are without nuclei, but always contain a slight amount of granular substance. Moreover, independently of the cells, granular matter is always perceptible on the addition of water.

Acetic acid, even when concentrated, scarcely produces any action on epidermis, even after it has been softened by water; but by prolonged boiling with concentrated acetic acid, the scales become isolated, and swell into extremely pale, distended, but still somewhat flattened vesicles, entirely devoid of granules or nuclei. According to Kölliker, the walls of the epidermic cells do not dissolve, but only those of the cells of the *rete mucosum.*

Acetic acid acts upon the substance of the nails in the same manner as upon the epidermis, only with less rapidity; it generally causes the nuclei of the cells to come beautifully and prominently into view.

Cows' horn is very little affected by the action of concentrated acetic acid, even after prolonged boiling; and the microscope

detects even still less alteration in whalebone or tortoise-shell that has been acted upon by this acid, although the former is converted into a gelatinous substance when boiled with the concentrated acid.

The epidermis very rapidly swells in concentrated *sulphuric acid*, exhibiting vesicular cells which become even more distended on the addition of water. The cells of the *rete mucosum* remain unchanged in cold sulphuric acid, but when boiled they are completely dissolved.

Concentrated sulphuric acid acts very slowly on the substance of the nails, but on the application of heat it brings into view, in the course of a few minutes, flat, polygonal cells, some of which are provided with nuclei.

It is only after the prolonged action of concentrated sulphuric acid for many hours that cows' horn gradually resolves itself into cells.

Whalebone is gradually converted, by this acid, into a mucous mass, in which the cell-membranes may be distinctly recognised.

Sulphuric acid exerts an equally inefficient action on tortoise-shell, and it is only after prolonged soaking or boiling with concentrated acid that cells can be detected in the gelatinously swollen mass; but even these are not isolated.

Concentrated *nitric acid* imparts a yellow colour to most horny tissues, and isolates the cells of some, without, however, bringing them distinctly into view.

These tissues have, as we already observed, been subjected to elementary analyses, after having been previously treated with alcohol and ether. In order to exhibit the analogy of their composition, we subjoin the empirical results obtained from the analyses of Scherer,* Mulder, Tilanus,† and van Kerckhoff.‡

	Epidermis.	Nails.	Horses' hoofs.	Cows' horn.	Whalebone.	Tortoise-shell.
Carbon	50·28	51·09	51·41	51·03	51·86	54·89
Hydrogen	6·76	6·82	6·96	6·80	6·87	6·56
Nitrogen	17·21	16·90	17·46	16·24	15·70	16·77
Oxygen	25·01	22·39	19·94	22·51	21·97	19·56
Sulphur	0·74	2·80	4·23	3·42	3·60	2·22

* Ann. d. Ch. u. Pharm. Bd. 40, S. 1-45.

† Scheik. Onderz. D. 3.

‡ Ibid.

These tissues differ also in the quantity of inorganic matter which they contain, but this difference does not vary much beyond 1$\frac{0}{0}$.

On boiling these tissues with a solution of potash, they generally, as we have already seen, become dissolved, with the exception of a comparatively very small residue: a large quantity of ammonia is developed, and the fluid contains much sulphide of potassium, the presence of which may be detected immediately after the first application of the alkaline fluid. When the alkaline solutions are saturated with acetic, hydrochloric, or other acids, precipitates are formed which, according to Mulder, differ in the character of their composition. These deposits exhibit the property of adhering together, and forming almost resin-like masses on being heated in water. Mulder includes them amongst his protein-oxides.

It will scarcely be necessary, after this notice of the reactions exhibited by these tissues, to remark that our knowledge of their chemical history is still too deficient, in a histological point of view, to afford any satisfactory reply to the questions already propounded. For although Mulder,* in his most recent communications, has calculated formulæ from his experiments, and has been consequently led to regard all these tissues as *combinations of protein or protein-oxides with sulphamide,* this hypothesis must certainly be limited to one of the main constituents of the horny tissue only, and cannot refer to the whole mass. Every horny tissue contains at least three different kinds of substances: namely, the substance of the cell-membranes, which is so difficult of solution in alkalies; the cell-contents, including the nucleus, which dissolve more readily in alkalies; and the granular matters, consisting by no means of fat solely, which remain after the complete solution of some of these tissues, and are wholly insoluble in alkalies. These three chemically-demonstrable matters can hardly be regarded as isomeric or polymeric, and could not, even in that case, be brought forward in support of the sulphamide hypothesis.

The principal portion of every horny tissue is formed, as we have already observed, by the cell-membranes; their contents and the nucleus being so subordinate to these that the elementary analysis of such a tissue must be regarded as giving an average expression for the composition of these cell-membranes. They do not behave, however, as if they consisted of a sulphamide compound, for micro-chemical examination shows that the ammonia

* Untersuch. übers. v. Völcker. H. 2, S. 272.

and sulphuretted hydrogen which we see developed on the macro-chemical treatment of these tissues with even very dilute alkalies, are not derived from the main substance—that is to say, the cell-membranes—but must originate in the cell-contents, or what is still more probable, in the connecting medium. If therefore a sulphamide of protein actually exists, it must be sought for in the tissue connecting the cells of the horny tissue, or, at all events, in their contents.

Although this connecting medium or true intercellular substance of the horny tissue can certainly not be detected by the microscope, it cannot possibly be wholly wanting; for independently of the fact that some of the above-described micro-chemical reactions testify to its existence, it would not be easy to understand how the cells formed in the mucous layer—the true matrix of this horny tissue—and driven forward, and gradually drying during the growth of the tissue, could entirely divest themselves of the adhering plasma. The cell-contents and the intercellular substance, the cell-wall and the nucleus, must stand in the active living cell, not only in a physical, but also in a chemical antagonism; and cannot possibly so far lose this diversity of character in the dried, atrophied, or disintegrated cell, as to form a chemically homogeneous substance, a simple sulphamide compound.

These remarks are by no means intended as an attack upon Mulder, whose labours, even on this subject, are very valuable.

The Hair.

If we are scarcely able to arrive at a clear or distinct view of the chemical relations of the morphological elements of the comparatively simple horny tissues, we are still less able to do so in reference to the far more complicated tissue of the hair. On examining a hair, we find that there are at least three morphologically different substances brought under our notice; namely, the cuticle, the cortex, and the medullary substance.

The cuticle of the hair consists of plates arranged in the manner of tiles, one above the other; these are rendered more visible, according to Donders and Kölliker, by the use of those reagents which cause the cortical substance of the hair to swell, as,

for instance, sulphuric acid, or caustic potash or soda. This scaly covering of the hair is not itself affected by such reagents, but by friction individual scales may be isolated, which then appear extremely transparent and quadrangular, and are devoid of nucleus or other contents, although they are generated from perfectly normal cells, as is seen by examining the root of the hair. Kölliker* draws attention to the fact that these epithelial scales on the hair differ from the other elements of the hair, and from all the constituents of other horny tissues, by their perfect insolubility in alkalies and concentrated sulphuric acid. We do not, however, agree with the supposition of Donders,† based on this mechanical relation, that these scales consist of a protein-compound.

The cortical or fibrous substance, constitutes, as is well known, the principal part of the hair. By the use of the reagents above referred to, namely concentrated and gently heated *sulphuric acid*, this substance separates into flat, long fibres, which again divide into long, very narrow plates, having a dark, elongated nucleus. After prolonged digestion with a dilute *solution of potash*, the cortical substance dissolves, with the exception of these long, spindle-shaped nuclei. Even if these plates did not so plainly bear the stamp of cell-formation, they would readily be recognised as cells by examining the corresponding part of the root of the hair. These plates gradually shorten, and the elongated nuclei become thicker towards the root of the hair, and at length, in the lower part of the root, we find oval or roundish cells with oval nuclei.

Kölliker's observations show that here also the chemical metamorphosis corresponds with the change of form, and that the cells of the cortical substance in the lower part of the root of the hair are not merely more easily affected by alkalies and concentrated sulphuric acid than the fibre-cells of the same substance, but that they become swollen, and are in part dissolved even by acetic acid, which produces no effect on the other cells. According to Kölliker, there are within the fibrous substance certain cavities filled with air, and also accumulations of pigment-granules, the quantity of which varies with the colour of the hair.

The inner portion of the hair is composed of the medullary substance, the nature of which cannot be recognised distinctly until the cortex has been rendered transparent by the action of alkalies. It consists of closely arranged rows of quadrangular, or

* Mikrosk. Anat. Bd. 2, S. 122.

† Vers. einer physiol. Chem. S. 572 [or English Transl. p. 523].

more rarely, round cells, which, after the above-mentioned treatment with potash, are seen to contain dark fat-like granules, in addition to a clear roundish or oval speck (the rudiment of a nucleus). Many of these roundish grey granules are observed between these cells in fresh hair that has not been treated with potash. Kölliker* has shown by several admirable experiments, that the dark granules which occur in coloured as well as in white hair, are for the most part mere cavities filled with air occurring between and in the dried medullary cells.

Such are the most important histological grounds on which a rational chemical examination of the tissue of the hair must be based. Unfortunately, however, chemists have hitherto been unable to analyse the hair when considered from this point of view. We have some admirable observations on this subject by Scherer† and van Laër,‡ who, although they have not investigated the chemical constitution of these parts in accordance with histological requirements, have yet exhibited the great analogy subsisting between the substance of the hair and other horny tissues, and have, moreover, successfully elucidated several important points involved in the inquiry.

Scherer's elementary analyses of the hair correspond with those of Laër, excepting that there is a slight difference in the amount of hydrogen:—

Carbon	50·65
Hydrogen	6·36
Nitrogen	17·14
Oxygen	20·85
Sulphur	5·00

Like most other horny tissues, the hair dissolves, with the exception of a few fine molecules, on prolonged digestion in a solution of potash, there being at the same time a development of ammonia. The solution yields on the addition of acetic acid a slight deposit, which is a less oxidised protein-compound than the far more considerable precipitate produced by the addition of a larger quantity of acetic acid; the latter, which is Mulder's deutoxide of protein, contains sulphur, and entirely agrees in its reactions with the substance which is obtained by the precipitation of the alkaline solution of other horny tissues on the action of

* Op. cit. p. 115.
† Ann. d. Ch. u. Pharm. Bd. 40, S. 58-63.
‡ Ibid. Vol. 45, pp. 147-183.

acids. Mulder also regards the substance of the hair as a sulphamide compound. No conclusions can be drawn from any analyses hitherto made in reference to the nature of the individual constituents of the hair, as, for instance, its connective tissue, cell-contents, &c.

Notwithstanding the closest search, Laër was unable to discover any special pigment in the hair, although the microscopical examination of the cortical substance of differently coloured hairs—that is to say, the existence of certain coloured molecules—indicates the presence of a definite pigment. It is, however, well known that white hair is especially rich in air, and that to this circumstance it mainly owes its glistening colour. Laër has further shown by numerous experiments on differently coloured hair that the iron which is present, and to which Vauquelin had drawn attention, exerts no influence whatever on its colour.

Laër found nothing but margarin, margaric acid, and olein in the fat extracted from hair; this fat had an odour of hair, or rather of sweat.

The amount of ash in the hair differs very much, although it does not bear any relation to the colour, or any other property of the hair. Laër found from 0·54 to 1·85% of ash in the hair, and from 0·058 to 0·390% of peroxide of iron, but he could not detect manganese; he found, however, some silica with phosphate of lime. Von Gorup-Besanez,* who has made a very elaborate examination of the quantity of silica in the hair, found that the hair of animals contained on an average a much larger amount of this substance than human hair (the latter containing only from 0·11 to 0·22%, whilst the former contained from 0·12 to 0·57%).

Wool and bristles do not differ essentially in their composition from hair: the chemical constitution of feathers has, however, been found by Scherer to differ very considerably from horny tissues generally, and from hair especially. He found as the mean of two analyses of the beard and the quill, 52·448% of carbon, 7·161% of hydrogen, and 17·787% of nitrogen. Gorup-Besanez found considerable quantities of silica in feathers. He has treated, in a most careful and complete monograph, of the influence of the most varied physiological relations, such as sex, age, mode of life, species, &c., on the quantity of silica in the feathers.

* Ann. d. Ch. u. Pharm. Bd. 66, S. 321-342.

Contractile Fibre-Cells.

We are especially indebted to the recent investigations of Kölliker* for a more accurate knowledge of those histological elements which have hitherto been included in their aggregation in the animal body under the name of *organic* or *smooth muscular fibres.* These cells commonly appear in the form of long fusiform narrow fibres, with finely attenuated extremities, frequently also in that of elongated, quadrangular, or club-shaped plates, whose margins are occasionally fringed. The majority exhibit, especially when acted upon by acetic acid, a prominent nucleus, which is either cylindrical or baton-like. The nucleus appears to be perfectly homogeneous, a nucleolus being scarcely ever found in it. The substance of the cell occasionally exhibits pale or dark granules, which are partially arranged in rows corresponding to the axis of the fibres, but in other respects this is also homogeneous. It cannot be decided with certainty whether it is surrounded by any special cell-membrane. These fibre-cells form by the lateral juxtaposition of their extremities the bundles of smooth muscle which are visible to the naked eye, and occur, amongst other places, in the intestinal canal. Kölliker divides the smooth muscle into the *pure* and *mixed* variety, according as the cells are arranged in larger quantities so as to form bundles and membranes, or are merely interspersed amongst other simple tissues; to the former class belong those which have been long known, and in which Henle† first recognised the presence of true fibre-cells, namely, the muscular coat of the lower half of the œsophagus, of the stomach and intestinal canal, the nipple, the bladder, the prostate gland and vagina. The coarser bundles of these muscles are likewise held together by connective tissue, but they are not so thoroughly intersected by it, and divided into separate fibrillæ, or smaller bundles of fibrillæ, as the mixed smooth muscles. The latter, which often appear as if they were scattered over connective tissue, embedded, as it were, in the elastic and nuclear fibres, were first shown by Kölliker ‡ to occur principally in the trabecular tissue of the spleen. They have since been discovered in many other compound tissues, which had been known as contractile and

* Zeitsch. f. wiss. Zool. Bd. 4, S. 48-87.

† Allg. Anat. S. 576.

‡ Mittheilungen der Zürich. naturf. Gesellschaft, 1847.

had been carefully examined with reference to their histological elements, without our recognising these cellular parts as identical with organic muscular fibres; especially in the tunica dartos, in the middle coat of the arteries, in the choroid coat of the eye, in the veins and lymphatics, in the corpora cavernosa, the prostate gland, the Fallopian tubes, the uterus and urethra; also in many mucous membranes, and especially around the intestinal villi (Brücke). In the trachea, the bronchi, the ureters and vasa deferentia, as well as in the internal muscular tunic of the testicle, they approximate more closely to the pure smooth muscles. Finally, the smooth muscles are never enclosed by a true sarcolemma.

These histological structures do not serve the animal organism by their physical properties like the elastic fibres, in conjunction with which they so frequently occur; but it is to them that those tissues, in which they were formerly either only imperfectly, or not at all recognised, owe their contractility *under the influence of the nervous system.* The admirable labours of Ed. Weber* have yielded us the most valuable information in reference to this subject, and have clearly elucidated the essential differences existing between the action of the contractile organs and that of the animal muscles. Weber has shown that in the case of almost all the organs which are provided with these cell-fibres, a mechanical or chemical irritant, such, for instance, as the employment of a galvanic current, generated by the rotatory apparatus, induced only a gradual, and, at first, a very limited contraction, which, however, became diffused, after a time, over a larger portion of the part in question. Neither the bundles touched by the pole, nor the parts depending upon the excited nerves, contracted in any very appreciable period after the application and interruption of the galvanic current, but the adjacent bundles became successively affected, and a movement was thus induced which did not finally disappear for a long time. Ed. Weber succeeded, both independently and in conjunction with E. H. Weber,† in detecting the contractions in veins and arteries of medium and small calibre in nearly the same forms as they occur in other organs. Kölliker‡ also has recently observed them in the blood-vessels and lymphatics of man.

Ecker§ and Kölliker|| have, however, fully shown, by com-

* Handwörterbuch der Physiologie. Bd. 3, Abth. 2, S. 1-122.

† Berichte der k. sächs. Gess. d. Wiss. 1849. S. 91-96.

‡ Zeitsch. f. wiss. Zool. Bd. 1, S. 257-260.

§ Ibid. pp. 218-245.

|| Op. cit. pp. 213-217.

parative demonstrations of the elements of motion in the lower animals, that this contractility, or property of contracting on the application of stimuli to the nerves, is not connected in the animal organism solely and exclusively with the fibre-cells of the smooth muscles, but appertains to other histological forms, such as amorphous membranes, tubes, vesicles, filaments, &c.

Our interest is naturally increased, as we here find ourselves dealing, for the first time, with a form of animal tissue which exhibits vital activity, or, in other words, moves through the influence of the nerves; and we find, moreover, that the chemical relations are here wholly different from those which we have hitherto noticed in those tissues of the animal organism which act solely by their physical properties.

The following remarks embody all that is known from my own observations, and those of Donders,* Schultze,† Paulsen,‡ and others, in reference to the *micro-chemical reactions* of these fibre-cells.

The most generally known of these is the action of *acetic acid*, which, when employed in a more or less diluted state, causes the substance of the fibre to swell, whilst it increases its transparency; the nucleus, which was pale and scarcely visible, now stands out more prominently, and commonly presents the appearance of a sharply outlined, baton-shaped, often somewhat bent and even twisted dark body, in which no nucleolus can be seen. According to Kölliker, acetic acid frequently causes the nuclei to contract in a slight degree; not unfrequently, it induces an augmentation in their breadth, rendering the nuclei paler instead of darker.

Concentrated acetic acid completely dissolves the fibre, until even the nuclei are gradually rendered indistinct. Fat-globules and molecular granules are then the only things to be discovered between the hyaline fibres of connective tissue.

Extremely dilute hydrochloric acid (1 part of anhydrous acid in 3,000 parts of water) behaves in almost the same way as dilute acetic acid, although, according to my experience, in a more decisive manner. The nuclei appear more distinct and dark, the substance of the cell becomes very pellucid, but at the same time assumes a curled or wave-like appearance; the nuclei lying in a curve of the fibre present, collectively, a crescentic appearance, and their extremities are in some cases twisted in opposite direc-

* Op. cit.
† Op. cit.
‡ Op. cit.

tions. By the prolonged action of the acid the substance of the cell is dissolved, leaving, in addition to amorphous granules, nothing but nuclei, which now, for the most part, assume somewhat the form of cucumber-seeds. The fibres of connective tissue, which are occasionally present, appear as very transparent, broadened, perfectly homogeneous bands. I was much surprised to find, on examining organic muscles which had been frequently washed in water, and macerated for a long time, that no nuclei could be rendered visible either by the dilute acetic or hydrochloric acid. (*F.* P. 14, F. 6.)* Henle† was led to infer, from the result of his experiments, that the superficial layer always soonest undergoes decomposition, and hence its nuclei are first destroyed.

The fibres shrivel up very readily in *concentrated hydrochloric acid*, but the nuclei are not rendered more transparent. After a prolonged exposure to the action of the acid, entire, finely striated bundles are brought into view. Water causes the fibres to swell, and form thick, sharply outlined strings, in which state they resemble the representations (or rather the diagrams) formerly made by histologists of normal organic muscular fibres.

Concentrated sulphuric acid renders the bundles of fibres more transparent and gelatinous; after the repeated addition of water the bundles contract, and again appear distinctly fibrous (Donders). No nuclei can be distinctly recognised, but I have frequently observed in preparations which had been treated with concentrated sulphuric acid, and after the repeated addition of water, the existence of coarse granules of an oval or irregularly rounded shape and isolated fat-globules, whilst the other histological elements had wholly disappeared.

The fibre-cells become somewhat contracted in *concentrated cold nitric acid*, and exhibit a curled appearance. The smaller bundles are divided into isolated fibrils of a pale yellow colour; no nuclei can be detected with certainty; the fibres of connective tissue remain smooth and narrow, and are not coloured yellow. The yellow colour appears in a remarkably beautiful manner in the fibre-cells on applying caustic ammonia to the object after it has been treated with nitric acid. The fibre-cells are perfectly dissolved in boiling concentrated nitric acid, whilst nothing appears in the fluid beyond a few scattered fat-globules.

A concentrated *solution of chromic acid* renders the bundles of smooth muscle so perfectly soft that they break up on the

* The abbreviation for Funke's Atlas, Plate 14, Fig. 6.

† Jahresber. der ges. Med. 1851, S. 44.

slightest pressure into greenish yellow, somewhat curled rods, which nowhere exhibit, with certainty, even a trace of a nucleus.

The prolonged action of a *dilute solution of soda* loosens, softens, and finally dissolves the bundles of fibres, leaving only fine long threads, which belong to the nuclear fibres. At the same time a number of coarse granules of a very irregular form are brought into view, whose chemical nature could not be closely investigated. There were no nuclei to be detected.

A *concentrated solution of potash*, after prolonged action, causes the almost total disappearance of the individual fibres, there remaining only rows of granules. On the addition of water, everything is dissolved excepting some minute filaments (in the same manner as by the action of dilute soda).

The fibre-cells undergo no visible alteration in a solution of moderately concentrated *carbonate of potash.*

On digesting a carefully prepared and well-washed portion of the muscular coat of the stomach of a pig for a prolonged period (from 18 hours to 3 days) in a solution of 6 parts of *nitrate of potash* in 100 parts of water, at a temperature of 30° or 40°, no essential change will be observed in the individual smooth muscular fibres; as in the case of carbonate of potash, they simply swell, and become somewhat more translucent. No nuclei can be discovered in either case. The muscular substance itself becomes somewhat harder.

Millon's reagent (see vol. i, p. 328) colours the whole mass of the bundles intensely red, but when seen under the microscope the individual fibre-cells do not appear very highly coloured.

An *aqueous solution of iodine* causes the fibre-cells to shrivel up, renders the nuclei less distinct, and imparts a yellow colour to the whole mass. The nuclei cannot be brought into view even by the repeated application of a dilute acid.

The bundles of fibrils become gelatinous in *concentrated phosphoric acid.* Under the microscope, fibrillation is still perceptible, which, however, becomes more distinct on the addition of water to the object. Here, too, we have a granular matter which does not, however, appear to contain a nucleus. The granules precisely resemble those which are brought into view on the addition of water, after the fibres have been treated with concentrated hydrochloric acid or a potash solution.

If the middle coat of the arteries, or the muscular coat of the stomach or intestinal canal, be treated with concentrated acetic acid, after having been cut in shreds and carefully rinsed, and

afterwards boiled for a considerable time in water in order to remove the gelatigenous connective tissue, a substance is dissolved which is precipitable both by yellow and red prussiate of potash. This may be again precipitated by neutralising the acetic acid; it contains a considerable quantity of sulphur.

The substance of the fibres of smooth muscle behaves towards very dilute hydrochloric acid (1 p. m.) in the same manner as Liebig* showed was the case with the striated fibres. (See note to vol. i, p. 359, on *Syntonin*, in the Appendix.) Thus, for instance, if the muscular coat of the stomach (of the pig), after being cut in shreds and thoroughly rinsed with water, be treated with hydrochloric acid of this dilution, the fibres of the smooth muscles become dissolved; on neutralisation of the acid, the solution behaves in precisely the same manner as the hydrochloric-acid solution of syntonin from striped muscle; the flakes, which gradually separate, dissolve very readily in an excess of an alkaline solution, and likewise in lime-water; this solution coagulates on boiling, like albumen; if, however, too much lime-water be added, the solution merely becomes opalescent, and it is not till it is neutralised with acetic acid that we have a copious curd-like precipitate. The original hydrochloric-acid solution of the fibrils is strongly precipitated by concentrated solutions of the neutral salts of the alkalies and alkaline earths; as, for instance, chloride of potassium, sulphate of soda, hydrochlorate of ammonia, chloride of calcium, and sulphate of magnesia.

I obtained precisely the same reactions on treating the well-washed middle arterial coat of the ox, the bladder of the pig, and the tunica dartos of the bull in a similar manner with dilute hydrochloric acid.

No sarcolemma can be chemically demonstrated in the organic muscles. Kölliker thought he could sometimes perceive indications of a cell-membrane in individual fibre-cells, but I have been unable to demonstrate its presence by any chemical reagents. The nature of the nucleus, which is insoluble in acetic and dilute mineral acids, has not yet been closely examined.

C. Schmidt† attempted some years ago to make an elementary analysis of smooth muscle (the large thoracic muscles of the Cockchafer and the adductor muscles of Anodonta cygnea), for the purpose of comparing its composition with that of striped muscular

* Ann. d. Ch. u. Pharm. Bd. 73, S. 125-129.

† Zur vergleichenden Physiologie der wirbellosen Thiere. Braunschweig, 1845, S. 32-69 [or Taylor's Scientific Memoirs, vol. 5, pp. 14-28].

fibre. He found that both kinds of muscle were perfectly identical in composition (52·3% of carbon, 7·2% of hydrogen, and 15·3% of nitrogen). We think that this coincidence scarcely proves anything more than the insufficiency of our elementary analyses; for supposing that the fibre-cells of smooth muscle were identical with the fibrils of striped muscle, it appears singular that the presence of sarcolemma and of tracheal ramifications in the one tissue, and of fibres of connective tissue in the other, (that is to say, of foreign substances, which cannot be removed by the most careful preparation,) should not induce any difference in the results of the analyses. We do not, therefore, think that we are justified in drawing a conclusion in favour of the identity of composition of the organic elements of motion from these analyses, although they were undoubtedly conducted in accordance with the best chemical methods.

If, as it would appear, smaller quantities of carbon and nitrogen have been found to be present in the tissues which have been analysed than in fibrin and albumen, it is more probable that the difference is rather owing to the amount of connective tissue and of chitin, than to a different composition of the contractile elements themselves.

We have, therefore, regarded it as more in accordance with the inductive method to institute, for the purpose of comparison, various elementary analyses of this substance, which is extractible from every contractile tissue by dilute hydrochloric acid, first precipitating it by a dilute solution of soda, and then extracting it with alcohol and ether. Although we have not so far deceived ourselves as to regard as perfectly pure this matter which, at all events, is mainly derived from the substance of the contractile fibre-cells, (such a supposition being controverted on chemical as well as histological grounds,) we yet believe that the analyses of this matter, obtained from different compound contractile tissues, are better adapted for comparison, and lead to more reliable results, than the analyses of the complex tissues themselves. And in point of fact, this cell-substance, which is soluble in water containing hydrochloric acid, invariably presented the same composition, whether it had been obtained from the muscular coat of the stomach of the pig, or the middle arterial coat of the ox, or the tunica dartos, or the bladder. It also appeared that this substance, which is derived from smooth muscular fibres, has the same composition as the analogous substance derived from striped muscular fibres, which was first obtained by Liebig and analysed by Strecker. As we shall have to consider more fully in another portion of this

work these analyses of my own, I will here limit myself to an enumeration of the mean results, merely for the purpose of comparison with the fibrin of the blood and that of the animal muscles; there were found on an average 53·84% of carbon, 7·30% of hydrogen, 15·81% of nitrogen, and 1·09% of sulphur.

This substance further corresponds with the protein-body extracted from striped muscle in being perfectly insoluble in nitre-water (containing 6% of $KO.NO_5$), as well as in carbonate of potash. Although the above-mentioned micro-chemical reactions demonstrated this point with tolerable certainty, the following experiments were additionally made. The muscular coat of the stomach was reduced to fine shreds and rinsed in water as long as any coagulable substance continued to dissolve; a portion of the rinsed mass was then digested for an hour in a solution of 1 part of carbonate of potash in 10 parts of water; the filtered fluid showed only traces of a dissolved protein-body. Another portion of the muscular coat, which had been freed from albumen, was digested for two days in the above-mentioned nitre-water at a temperature of 37°; at the end of that period there was not a trace of any substance coagulable by heat or acetic acid.

As this substance appears, according to the present state of our knowledge, to be altogether peculiar to contractile fibre, as it differs essentially from the fibrin of the blood, and lastly, as it does not merely occur in the true muscles, we have thought that it would be desirable to distinguish it from ordinary fibrin by some peculiar designation, and we have suggested as appropriate the name of *syntonin* (from *συντείνειν*). [The chemical and physiological characters of syntonin are described in the Appendix.—G. E. D.]

It is probably a very significant fact, that the more active organs of the animal body are bathed in a fluid which differs very essentially fron an ordinary transudation from the blood, or from the blood-plasma itself. Berzelius long since directed attention to the muscular fluid, and Liebig's admirable investigation of this subject is well known. According to Liebig's discoveries, a fluid differing in every respect from the plasma of the blood surrounds the fibres of the striped muscles; and the same is the case with the fibre-cells of the smooth muscles. M. S. Schultze* found, on examining the middle coat of the arteries, that it was permeated by a fluid very rich in casein. He found in 100 parts of the well-dried annular coat of the thoracic aorta from 17·4 to 23·1% of soluble consti-

* Ann. d. Ch. u. Pharm. Bd. 71, S. 277-293.

tuents, amongst which there were 7·24 parts of casein. He also found in the middle coat of the carotid, which, as is well known, contains a smaller quantity of elastic fibre, but far more contractile fibre-cells than the aorta, 39$\frac{0}{0}$ of soluble constituents, of which 21 parts were casein. Moreover Schultze found that this interstitial fluid had a faintly alkaline reaction, and contained in addition to the casein and salts, small quantities of two substances, one of which was coagulable, and the other non-coagulable by heat.

My own observations on the juice permeating the contractile tissues have shown that the fluid obtained from the muscular coat of the stomach of the pig has a distinctly acid reaction, although not in so intense a degree as that derived from the striped muscle; the analogous fluid of the middle coat of the arteries (the ascending and descending aorta, and the carotid of the ox) reddened litmus paper slightly, but quite decidedly. The fluid from the tunica dartos exerted no reaction on vegetable colours. Schultze found that the juice of the middle coat of the arteries was alkaline, which may be owing either to the admixture of the alkaline fluid of the cellular tissue, or to the occurrence of incipient decomposition. The middle coat of the arteries and the tunica dartos yield more casein and less albumen than the muscular coat of the stomach of the pig; the latter is as rich in albumen as is the juice of the animal muscles.

Creatine occurs in much smaller quantity here than in the juice of the striped muscles; but as the inadequate amount of this substance precluded the possibility of making any elementary analysis, the crystallometric determination constituted the only evidence of its presence. Besides a small quantity of lactic acid, we find acetic and butyric acids. The ratio of the potash to the soda was as 38 : 62 in the juice of the smooth muscles of the stomach, and as 42 : 58 in that of the middle coat of the arteries. The soluble phosphates were to the insoluble as 82 : 18 in the muscular fluid of the stomach, and as 79 : 21 in the fluid of the middle coat of the arteries.

Siegmund* has recently found creatine, acetic acid, and formic acid in the juice of a pregnant uterus; and Walther † has, under my superintendence, extended the above-mentioned micro-chemical investigations regarding the fibre-cells, and the chemical analysis of the juice by which they are moistened.

All these relations, which are at the present time undergoing a

* Verh. der phys.-med. Ges. zu Würzburg. Bd. 3, S. 50.

† Diss. inaug. med. Lips. 1851.

more accurate investigation, show that there exists, at all events, a very great analogy between the juice of the striped muscles and that of the fibre-cells. If we concur in the doubts expressed by some of the most distinguished histologists regarding the existence of these fibre-cells in the middle coat of the arteries, in which Kölliker believes he has found them, it would, at all events, seem to be proved, in regard to the chemical view of the case, that the fibrils of the striped muscles, like the smooth muscles and the contractile tissues, not only contain a solid substance which is chemically identical in all, but that this textural element is invariably surrounded by a juice which differs essentially from all other animal juices by its acid reaction, the abundance of its potash-salts and phosphates, and by its containing creatine, &c. It remains for a more exact investigation to establish with greater precision the differences which the provisional analyses indicate between the constitution of these juices in the different contractile tissues.

Although we have already sufficiently indicated the course to be pursued in the investigation of contractile tissue, we will briefly review the mode of proceeding. If we are once assured that the object which we are examining is a tissue composed of various histological elements, which, moreover, is permeated by a fluid differing in all respects from the blood-serum,—whether such contractile tissue be obtained from the middle arterial coat, the muscular layer of the intestine, the urinary bladder, the tunica dartos or the uterus,—our first endeavours should of course be directed to the removal of the unimportant constituents from the fibres of the smooth muscle. Unfortunately, we are quite unable to obtain perfectly pure fibre-cells free from nerves, connective tissue, and nuclear and elastic fibres; we are therefore compelled to have recourse to various indirect means of obtaining a knowledge of the chemical nature of this histological element. When the tissue has been carefully reduced to minute shreds, and rinsed in lukewarm water until no trace of organic matter is longer visible in the fluid that is poured over it, two methods present themselves for our choice in preparing the substance of the fibre-cells for chemical examination. We may dissolve either the connective tissue or the fibre-cells; either method, however, is open to serious objections. No other solvent than boiling water should be used for dissolving the connective tissue when an albuminous tissue is present; and, even then, we only attain our object in a most imperfect manner; for, in the first place, the fibrinous substratum of the cells is reduced to a state of coagulation, which

precludes the possibility of separating this substance from the nuclei of the fibre-cells; secondly, the fibre-cells themselves are attacked by the prolonged boiling which is necessary for the purpose of effecting as completely as possible the solution of the connective tissue, (a substance, corresponding to Mulder's tritoxide of protein, dissolving with the gelatin, as Schultze formerly remarked;) thirdly and lastly, notwithstanding all boiling, the nuclear fibres of the connective tissue remain undissolved (as has been often already mentioned), and even when no true elastic fibres are interspersed amongst the contractile tissue, constitute a residual mass which cannot be regarded as a chemically pure body. The coagulated substance of the smooth muscles does not dissolve readily in alkalies, and cannot, therefore, be very perfectly separated from the substance of the nuclear fibres, as this also partially dissolves in alkalies, more especially on the application of heat. The quantity of sulphur contained in the contractile fibre-cells cannot therefore be determined with certainty by this method, nor is the method of dissolving the substance in alkalies, and precipitating it by acids, to be unconditionally recommended; if, however, we would analyse for its sulphur the substance after being only boiled in water, without having been previously dissolved in alkalies, we should in every case find too small a quantity of sulphur; for the nuclear fibres augment the matter which is free from sulphur, and some of the sulphur of the substance also escapes on boiling it in the air.

It is better, therefore, for these reasons to endeavour to dissolve the substance of the fibre-cells, and we may employ as a solvent dilute alkaline solutions, moderately dilute acetic acid, or water containing hydrochloric acid. I have found that the most efficacious of these three solvents is the very dilute hydrochloric acid (containing from 0·1 to 0·5% of the acid). A dilute solution of soda renders the connective tissue too gelatinous, and very probably also dissolves some of the nuclear substance of the contractile fibre-cells, and makes the determination of the sulphur uncertain. Acetic acid is better, but the first of the objections advanced against the use of the soda solution exists also in the case of this acid. The hydrochloric-acid solution must be regarded as a tolerably pure solution of the substance of the cells of the contractile tissue, as the connective tissue, the nuclear fibres, and the nuclei of the fibre-cells themselves remain undissolved. The substance of the fibre-cells is thrown down from this solution by careful neutralisation in the form of a soft gelatinous mass, which is

perfectly adapted for the determination of the sulphur and for the elementary analysis generally, after it has been extracted with alcohol and ether. The substance composing the nuclei of the fibre-cells cannot be obtained in an equally pure state, since its best solvent is a dilute solution of soda, which always dissolves some of the connective tissue, or, at all events, occasions the gelatinous parts to pass through the filter.

We abstain from making any remarks on the method of examining the parenchymatous fluid, partly because we have already frequently spoken of the mode of determining the individual constituents of the animal fluids, and partly because we shall have occasion to revert to this subject under the head of the Striped Fibres.

Transversely Striped Muscular Fibres.

These textural elements, which have also been termed *animal* (Breschet), or *articulated* (Treviranus) muscular fibres, or *bundles of contractile fibrils* (Kölliker), are peculiar to those organs of motion which, at least to a certain extent, are *subject to the will.*

If we examine any muscle (as, for instance, one of the abdominal muscles) in both longitudinal and transverse sections, we perceive, even with the naked eye, that it consists of a more or less considerable number of parallel, longitudinally striped bundles (the secondary muscular bundles), which are surrounded by connective tissue (*perimysium internum*), serving to unite them together. In this connective tissue we may trace, on a careful examination, a few blood-vessels and nerves; but when we examine these striped bundles under the microscope, we perceive that the longitudinal stripes are dependent on yet finer bundles, which may be recognised under higher magnifying powers as roundish, irregularly flattened cylinders or strings, whose transverse section occasionally appears hexagonal, and which exhibit distinct transverse striation. A more careful examination of these very fine, transversely striped bundles (primitive muscular bundles) shows that they consist of closely approximating, necklace-like filaments, which are closely surrounded by a homogeneous smooth investment (*sarcolemma*). This investing membrane of the different primitive bundles is held together by filaments of connective tissue;

between the sarcolemma of the different bundles we find the well-known vascular network of the muscles, with its generally rectangular meshes, and the tortuous windings of the nerves. It is not a settled point whether the sarcolemma in the developed muscle contains nuclei; that is to say, whether the nuclei, which are apparently perceptible in it, appertain to it, or whether they lie under it, and belong to the muscular fibrils of the primitive bundles, and therefore to the contents of the sheaths of sarcolemma; at all events, we may perceive in the sarcolemma roundish nuclei, frequently resembling drops of oil, or, more rarely, having a spindle-like form, of which some at all events, according to Schwann and Kölliker, are situated between the sarcolemma and the muscular fibrils, but are not intimately connected with any of these parts. We find, as has been already observed, that the substance inclosed in the sarcolemma always presents a strongly marked transverse striation, and generally a less distinct longitudinal marking; so that the primitive bundles might just as readily be supposed to consist of superimposed discs (Bowman) as of long, transversely striated fibrils. In muscles, however, which have been submitted to chemical treatment (whether simple boiling or the action of reagents), we very frequently see a separation or disintegration of the contents of the sarcolemma into constricted filaments, which has led most histologists to regard these contents as composed of fibrils. It is very generally believed that the constrictions of the transversely striated primitive fibrils stand in the closest relation to the function of the muscles; on making a microscopical examination of the muscles of just killed or still living caterpillars, we perceive the dark stripes approach one another, and again separate. In paralysed muscles (which have not yet undergone fatty degeneration) these stripes are observed to be more widely separated from one another than in healthy muscles, &c.

Although several very admirable investigators will not admit that these observations afford sufficient evidence of the essential part which these constrictions of the elementary fibrils take in muscular contraction, the constrictions, or, perhaps, more correctly speaking, varicose dilatations, which are so constantly observed in this group of animal fibres, cannot be wholly purposeless or accidental; for, granting that our theory of the contraction of the fibrils is very complicated, the want of homogeneity in the fibres must exert some influence on their contraction. The elementary fibres are assuredly not formed of an entirely homogeneous substance; for, in the first place, we occasionally see the muscular fibre

break up transversely into discs (Bowman*) or into parallelopipeds, and each separate fibril into smaller linear sections, and, finally, into serially arranged granules (see vol. ii, p. 127). The continuity of the elementary fibres is therefore readily destroyed in the direction of the contractions. On the other hand, the muscular fibrils, as I perceived long before I was acquainted with Bowman's observations on the subject, undergo certain alterations of form by which they are either shortened or lengthened, when subjected to the action of water and other substances. I treated the muscular fibres of the extremities of tolerably developed embryos of the common mouse (*mus domesticus*) with different chemical reagents; I found that the addition of water had the effect (as Bowman has very often observed) of rendering the striation more indistinct, and sometimes even causing it wholly to disappear; but when very saturated solutions of neutral salts, such as chloride of calcium, sulphate of soda, hydrochlorate of ammonia, or of sugar, &c., were added, the transverse striæ which were originally at a relatively great distance from one another, came nearer together, the shortening being readily appreciable by the micrometer. The transverse striæ themselves appeared to be sharper and more distinct, but separated again more widely from one another when the saline solution was washed out as much as possible by water; and although their outlines grew fainter, they could not again be made wholly to disappear. This observation, which was frequently repeated, proves, at all events, that the muscular fibrils have a different capacity for imbibition at their varicosities and constrictions, depending upon a difference in the aggregation of their smallest mechanical, if not chemical, particles. The elementary fibre of the animal muscles cannot therefore be considered as homogeneous; nor can we regard the phenomena which are produced on the application of saline solutions, as the effect of simple contortions of the fibres, such as Henle observed in connective tissue.

If the physical examination of the muscular fibrils shows that they are not simple, homogeneous, partially folded strands, this is still more distinctly proved by a chemical investigation, as it destroys the fibres; for whatever may be the reagent employed, the fibrils are always unequally dissolved. First of all, there are formed small filaments resembling vibriones, which, together with fat-globules, resolve themselves into a number of molecular, often serially arranged granules. If we regard the primitive fibres as not

* Philosophical Transactions for 1840, p. 457.

homogeneous, this must be still more the case with the primitive bundles. We have already referred to the nuclei on the surface of the muscular fibres; the elementary fibrils themselves, however nearly they approximate to one another, or however closely they are invested by the sarcolemma, are yet connected by an intermediate substance, which is itself of a double nature; for, in the first place, certain distinguished microscopists have observed, on transversely cutting through a muscular fibre, that there is a granular and molecular substance lying between the extremities of the individual fibrils; and secondly, we can scarcely seek for the juice, which has been so admirably investigated by Liebig, elsewhere than within the sarcolemma of the primitive bundles, which it appears to permeate.

We must, therefore, separate our chemical investigation of the animal muscles into several sections; of these, passing over the ever-present connective tissue of the perimysium as not at present concerning us, the numerous ramifications of blood-vessels, the nervous twigs, and the sparingly scattered lymphatics, the micro-chemical investigation of the sarcolemma and of the cylindrical bundles of fibrils within it demands our special attention; from this we will pass to the macro-chemical reactions, which can be exhibited with muscular tissue, terminating our inquiries with the examination of the parenchymatous juice.

Very dilute *acetic acid* (1 part of acetic acid in 5000 parts of water) causes the primitive bundles of the muscles to swell very rapidly, and to assume an extremely pale colour; after a prolonged action of two or three or even four days, we observe that the bundles are much swollen, that the transverse striæ are very distinct, and approximate more closely to one another, and that the nuclei parallel to the long axis of each bundle are very narrow, elongated, granular, and not sharply defined; many of them are constricted at four or five points, whilst others protrude with the muscular substance from the sarcolemma, and are scattered about transversely and obliquely in relation to the axis of the muscular bundles. There is never any appearance of longitudinal striæ (indicating the existence of primitive fibrils) in the muscular substance itself; on the other hand, a transverse striation may often be distinctly perceived. At the cut extremities of several primitive bundles we may frequently recognise portions of muscular substance, corresponding to an individual transverse striation, and which, without having any distinct form, such as Bowman has delineated, clearly show the division of the muscular fibre in the direction of the

individual transverse striæ; under favourable illumination, and by the help of the diaphragm, the flat sections are seen to present a net-like appearance, resembling lines which intersect one another at acute angles, and are somewhat swollen at the points of intersection. The transverse separation of the muscular fibres may often be recognized by the fact, that the half only of a disc corresponding to the transverse cleavage is torn off, whilst in some cases one of the transverse discs of a muscular fibre is loosened and coiled back on itself; or again, a muscular fibre is somewhat bent and torn up at its convexity into separate transverse discs, causing them to diverge like the leaves of a badly bound open book. (*F.* P. 15, F. 4.)

Concentrated acetic acid produces the same effect after from 5 to 10 hours' action, as the dilute acid does in a much longer period.

The *sarcolemma* is not altered either by dilute or concentrated acetic acid; at the parts where it has been deprived of its contents, it presents the appearance of a structureless membrane without nuclei, but interspersed at different points with fat-globules.

Very *dilute hydrochloric acid* (1 part of acid in 12,560 parts of water) produces nearly the same effect on the muscular bundles as acetic acid, rendering them paler, whilst the nuclei come prominently forward; the muscular fibres do not, however, swell to so great an extent as when dilute or concentrated acetic acid is used; the transverse striations are sharply marked, but a transverse cleavage of the fibres is not so frequent; there is no appearance of longitudinal striations (primitive fibrils). The mode of action of a less dilute hydrochloric acid will be considered at a subsequent page.

Donders* maintains that by prolonged digestion in dilute hydrochloric acid, the sarcolemma (at all events, in the primitive bundles of the heart) is rendered very distinct.

Concentrated hydrochloric acid converts moderately sized pieces of muscle, after a short time (8 hours), into a viscid mass, which can be easily stirred in the fluid surrounding it. We discover under the microscope, that the fluid contains rather short parallelopipeds, having a very distinct and often sharply defined transverse striation. Although longitudinal striæ may be detected here and there in the fibres, the primitive bundles are only torn or cleft in a transverse direction; but whilst the transverse striæ always follow a tolerably parallel course, they frequently exhibit several

* Nederlandsch Lancet. 3 S. 1 J. S. 559.

interstices or cavities which do not extend through the whole bundle, but give it the appearance of being strongly marked at intervals by black lines. The transverse striæ in many of these parallelopipeds are only indicated by the presence of fine granules arranged in a more or less decidedly parallel direction. Some of these strongly granulated fibres appear as if they had been eroded on their longer sides; but there is never any appearance of the bundle being divided longitudinally. The substance of the fibres is rendered intensely yellow by an aqueous solution of iodine, and the addition of water cause it to swell to a trifling extent only. Nuclei and sarcolemma can only be recognised at occasional spots, and for the most part after the addition of iodine. (*F.* P. 15, F. 3.)

In *concentrated nitric acid* the primitive bundles dissolve into yellowish parallelopipeds with a sharply defined transverse striation, after an interval of time varying from one to ten hours. The bundles are cleft only in a transverse direction, exhibiting larger or smaller openings between the striæ, in the same manner as when they are exposed to the action of concentrated hydrochloric acid; that is to say, two adjacent transverse discs are more separated from one another at one point than at another, and are only partly in contact. At some of the smaller sections of the bundles, all the transverse discs diverge from one side in a brush or tuft-like manner. There is never any trace of longitudinal striation. (*F.* P. 15, F. 2.)

Very *dilute nitric acid* exerts the same action as dilute hydrochloric acid.

In *concentrated sulphuric acid*, the muscular fibres, after from ten to thirty hours' action, are resolved into a reddish purple viscid fluid, in which, at a first glance through the microscope, we can only perceive longer or shorter filaments; a more accurate examination, however, shows that they are very thin hone-shaped or fusiform plates. The red colour disappears on the addition of water, when a greyish yellow coagulum is deposited, which appears perfectly amorphous, as seen under the microscope, exhibiting merely granular patches, in the same manner as we commonly observe with the coagulated protein-bodies.

Sulphuric acid, when somewhat diluted, exerts precisely the same action as concentrated hydrochloric acid, bringing the transverse striæ very distinctly into view. The longitudinal striæ which Mulder and Donders saw in these cases, I could scarcely recognise with any degree of distinctness even after the prolonged action of this acid.

Very dilute sulphuric acid acts in the same manner as acetic acid, or extremely dilute hydrochloric acid.

A concentrated solution of *chromic acid* causes the muscular fibres to be resolved, after prolonged action, into parallelopipeds of an intense yellow colour, some of which exhibit a sharply defined longitudinal striation without any perceptible transverse striæ, whilst others are characterised by the most beautiful and delicate transverse striation. Both in the longitudinally and transversely striated portions we frequently find four, five, or even more transverse rents and clefts, but never any cleavage in the longitudinal direction. Many of the fibres are broken up into irregular flakes; but the muscular fibres do not in any case appear to resolve themselves into definitely formed morphological elements. The sarcolemma is gelatinous and finely granulated.

When a muscular fibre has been exposed to the prolonged action of a saturated solution of *bichromate of potash*, the transverse striæ stand sharply out, whilst the fibre corresponding to them is torn at different spots, or exfoliated in the individual transverse striæ.

When small carefully prepared portions of muscle are digested for a long time at a temperature of from 30° to 40°, in a solution of six parts of *nitrate of potash* in 100 parts of water, no solution of one or other of the elementary parts of the muscular tissue can be observed. The transverse striation is generally visible in the primitive bundles, while the longitudinal striæ are rendered far more conspicuous. I know of no menstruum which so clearly exhibits the longitudinal cleavage of the muscular bundle projecting from the sarcolemma. This projecting portion splits in the form of a tuft into diverging, primitive longitudinal fibres, which individually exhibit distinct transverse striæ. These, however, do not exhibit the form of varicose dilatations of the fibrils, but present the appearance of clear and light spots, which succeed one another in a very regular manner, and have the same transverse diameter. The fibres appear as if composed of linearly arranged parallelopipeds of translucent but not transparent substance. (*F.* P. 15, F. 4.)

Pieces of muscle, when exposed for a prolonged period to the action of *sub-nitrate of mercury* (with the nitrite), are converted into a violet coloured, hard brittle mass, which admits of being reduced to a nearly purple-coloured powder. When examined under the microscope, the muscular bundles appear in the form of pale bluish red parallelopipeds, which exhibit the most delicate and sharply defined transverse striation. In thin sections, cut

somewhat obliquely to the axis of the muscular bundle, we remark detached lamellæ arranged upon one another in such a manner that the muscular cylinder or bundle appears to consist of plates or discs superimposed on one another. The sarcolemma, which we can often distinctly recognise here, remains as free from colour as the interspersed connective tissue.

A moderately dilute solution of *carbonate of potash* renders the muscles hard and rigid, as was especially shown by Virchow. On making a microscopical examination of muscle that has been hardened in this manner, the bundles are observed to be somewhat swollen, presenting no appearance of longitudinal striæ; the transverse striæ are fine and sharply defined; the cut surfaces of the bundles are generally very distinct; but wherever the preparation has been torn or pressed in its adaptation for microscopical purposes, the extremities exhibit exfoliated and partly somewhat recurved lamellæ; but I have never succeeded in obtaining the round laminæ in the isolated state in which Bowman has obtained his discs (as, at least, would appear from his diagrams). Pieces frequently presented themselves resembling sections of concentrically arranged circles; the lamellæ were in some cases only faintly granulated on their broad surfaces, in others sharply punctated. The sarcolemma was indistinct; no nuclei were visible.

After the prolonged action (varying from eight to seventy-two hours) of an extremely dilute *solution of soda* (consisting of one part of the alkali in 8500 parts of water), the muscle was reduced to a thoroughly gelatinous mass; the primitive bundles were for the most part dissolved, and those which were not thoroughly dissolved exhibited a faint longitudinal striation, caused by the regular deposition of granules in rows, so that the whole resembled tuberculous, stringy, bronchial mucus, which, on the addition of water, frequently exhibits a similar appearance of granules, arranged so as to imitate fibres. There was not a trace of nuclei, or of transverse or longitudinal striation. Here and there were remarked empty portions of sarcolemma, which appeared either perfectly hyaline or faintly granulated, and bore a close resemblance to the hyaline cylinders in the urine in Bright's disease, which correspond to the *membrana propria* of the tubes of Bellini. It is worthy of notice that these cylinders of sarcolemma have generally a much smaller diameter than the original primitive bundles, which furnishes a proof of the great elasticity of the sarcolemma, and of its close approximation in its normal state to the cylindrical bundles of fibrils. The elements of the perimysium admit, moreover,

of being most admirably brought into view by the action of a dilute solution of soda.

A *concentrated solution of potash* causes the primitive bundles to swell and become transparent, rendering the transverse striation less distinct. Its prolonged action causes the disintegration of the bundles into parallelopipeds, and renders the transverse striæ less distinct, and only to be detected by the appearance of parallel rows of granules; here and there longitudinal striæ may be seen, which, in conjunction with the granules of the transverse striæ, form necklace-like filaments, such as Mulder and Donders have already noticed. Nuclei are not always to be observed, or in every kind of flesh; but wherever they occur, they are observed to be much swollen, rather oval than fusiform, and granulated. On the addition of water everything is dissolved, with the exception of portions of the sarcolemma, which are reduced in their transverse diameter, and the nuclear fibres.

When a very dilute solution of potash or soda is allowed to flow over a fresh preparation under the microscope, the muscular bundles become much swollen, the transverse striation disappears, a partly filamentous and partly granular mass projects from the sarcolemma, whilst, as Kölliker observed, the nuclei are simultaneously brought into view. The nuclei commonly swell very considerably, become roundish, gradually lose their clear outline, and finally altogether disappear.

An *aqueous solution of iodine* imparts an intense yellow colour to the primitive bundles, and more frequently causes the longitudinal striæ to appear than any other reagent; it does not, however, cause the tranverse striæ wholly to disappear, but often renders them somewhat less distinct.

Fragments of muscle which have been repeatedly washed with distilled *water*, and exposed to strong pressure, either entirely lose their transverse striation, or show only faint indications of it, whilst the longitudinal striation is peculiarly visible. If these muscular bundles, after being rinsed with water, are treated with a very concentrated *solution of chloride of calcium*, the transverse striæ are often brought very prominently into view; the primitive bundles increase transversely; the terminal surfaces of the torn primitive bundles are very irregular, and do not correspond either with the transverse or the longitudinal striations; most of them have a digital form with convex ends, as if the soft mass of the fibrils had been compressed by the swelling of the sarcolemma, and had somewhat protruded from it. The sarcolemma and nuclei

can seldom be clearly distinguished. A saturated solution of *carbonate of potash* acts upon the macerated muscles very much in the same manner as chloride of calcium; the individual bundles have a very sharply defined outline, and are enlarged transversely; the longitudinal striation almost wholly disappears, and leaves the transverse striation so sharply defined as to make the dark striæ appear much thicker than the lighter ones. *Concentrated nitric acid* certainly causes the transverse striæ in the macerated primitive bundles to reappear; the dimensions of the latter are considerably diminished transversely.

Dilute hydrochloric acid, such as that employed by Liebig,* for the extraction of muscle-fibrin (1 p.m. H Cl), causes the sarcolemma to come prominently into view. Pieces of muscle which have been thus treated show an amount of connective tissue, and more especially of nuclear fibres, far exceeding what one would expect to meet with, judging from the ordinary modes of examining muscular tissue. As has already been observed, the individual portions of sarcolemma bear a strong resemblance to the cylinders in the urine in Bright's disease; they have a much smaller diameter than the primitive bundles which they surround. The smaller portions of sarcolemma are entirely empty, and are simply interspersed here and there with granules of various sizes. In the longer pieces of sarcolemma the nuclei appear irregularly disposed, near and amongst one another, and, in addition to the nuclei and granules, there appear at intervals bodies similar to masses of fat, sometimes resembling the pulp which protrudes from the nervous fibres, or at other times appearing as very small granular cells. The true membrane of the sarcolemma is extremely hyaline, and can generally be only clearly made out by the aid of very good illumination and simultaneous shading with the diaphragm. When these preparations are acted upon by a saturated solution of *carbonate of soda*, the nuclei and a portion of the granules disappear, and the sarcolemma becomes almost more hyaline. *Concentrated nitric acid* also causes the nuclei to disappear, but colours the sarcolemma yellow, whilst the connective tissue remains uncoloured. This difference of colour is rendered very conspicuous on saturating the acid with potash. *Chromic acid* also imparts to the sarcolemma a very beautiful yellow colour, whilst, at the same time, it contracts it to so great a degree that the diameter is scarcely one-third or one-fourth of that of the original primitive bundle; the nuclei disappear entirely. On adding a very *dilute*

* Ann. d. Ch. u. Pharm. Bd. 73, S. 125-129.

solution of soda to the fibres which have been treated with dilute hydrochloric acid, the nuclei swell in the sarcolemma from which the fibrils have been thus removed, and very rapidly disappear; the very hyaline sarcolemma continues to exhibit a faintly granulated appearance.

These micro-chemical investigations show that the three morphological elements which we distinguish in the primitive bundles of muscle differ chemically from one another, constituting respectively the true substance of the fibrils, the substance of the nucleus, and the sarcolemma.

The chemical properties of the substance of the fibrils (syntonin) have been already glanced at in p. 68 [and will be further considered in the Appendix to this volume]. The micro-chemical investigations already made on the substance which may be extracted from the muscles with dilute hydrochloric acid, lead us to concur in Liebig's view of this being the matrix of true muscular fibre. We have already observed that the primitive bundles of muscle, even when they have been digested for a prolonged period in a solution of nitre at a temperature of 30° or 40°, do not exhibit any change under the microscope which can justify us in believing that there is the slightest partial solution of the finest muscular fibrils.

As, however, these experiments were mostly made with the flesh of oxen and calves, and as the fibrin of the blood of oxen is, as is well known, nearly insoluble in a solution of nitre, whilst that of other animals is dissolved very readily after a short digestion (see vol. i, p. 351), the precaution was taken to select swine's flesh, which was freed as far as possible of its fat (the blood-fibrin of the pig being very readily soluble in a solution of nitre), and, after cutting it into very fine pieces, to rinse it with distilled water until the fluid that was pressed out of it exhibited no traces of albumen. After this mass had been freed as far as possible from soluble protein-bodies, it was digested for two or three days in a solution of nitre, of the strength already specified; but there was no trace of any dissolved protein-substance which was either coagulable by heat, or precipitable by acetic acid or any other reagent. The syntonin contained naturally in the muscular fibrils is, therefore, quite as insoluble in a solution of nitre as that which is artificially obtained from the muscles by means of hydrochloric acid, &c.

We are led to conclude from the micro-chemical reagents already indicated, that the *substance of the nuclei* inclosed in the sarco-

lemma does not differ very much from syntonin. It is dissolved with nearly equal rapidity by dilute alkalies; it swells in concentrated alkalies, dissolving very rapidly when water is added. It behaves in precisely the same manner as the substance of the fibrils towards concentrated acids, as, for instance, nitric acid. A difference is observed in the case of acetic acid, and of the mineral acids, when extremely diluted; for, although these reagents render the nuclei more distinct, they exert a certain amount of solvent action upon them; the nuclei wholly disappearing after a prolonged digestion in dilute acids, leaving only some fine molecules, which probably consist, for the most part, of fat.

We may readily convince ourselves that the clots or granules visible in the sarcolemma which has been emptied by acids or alkalies, consist for the most part of fat, either by repeatedly shaking with ether the remains of muscular fibres that have been treated with a dilute solution of soda, or, better still, by repeatedly boiling them in alcohol; for we can not only recognise the presence of fat in the ether or alcohol, but fewer clots and granules can be detected under the microscope in the less granulated sarcolemma.

Kölliker* and Scherer have demonstrated that the *sarcolemma* does not consist of connective tissue, and that it yields gelatin on boiling; and this view is confirmed by the above-mentioned micro-chemical reactions, which show most obviously that its chemical substratum has no affinity whatever to protein-bodies. If we bear in mind that neither acids nor alkalies cause the sarcolemma to lose its elasticity, which, as in the case of elastic tissue, resists alike the action of alcohol and boiling, we shall be led to concur in Kölliker's opinion, that the sarcolemma contains a substratum analogous to the elastic tissue; but it is by no means easy to determine whether, like elastic tissue, it acquires a yellow colour from the action of concentrated nitric acid. Kölliker was unable to produce any yellow colour in the sarcolemma of the Axolotl by means of nitric acid. As may be inferred from the above-described micro-chemical relations of nitric acid towards the muscular fibre, the sarcolemma cannot be isolated and distinguished in the flesh of the higher animals; but the yellow colour produced in the elastic tissue by nitric acid is not so distinctly visible on a microscopical examination as in the protein-like tissues, and on that account the microscope can afford no reliable information in reference to this point; when it occurs on a large scale, the elastic

* Mikrosk. Anat. Bd. 2, S. 250.

tissue is certainly coloured yellow by nitric acid (especially on the addition of potash), and this is also the case in the empty sheaths which remain after the repeated treatment of muscular fibre with a dilute solution of soda, and a thorough rinsing with water; but we are yet without any conclusive proof that these tissues were wholly free from all protein-like substances when they were submitted to the action of the nitric acid, and it would be extremely difficult to prove that such was the case.

We have already frequently referred to Liebig's admirable investigation of the fluids contained in the flesh; these researches have not only tended materially to elucidate a very obscure subject of inquiry, but have also thrown considerable light on nearly all departments of physiological chemistry. We have now merely to consider generally the composition of the juice extracted from the striped muscles, and to enlarge somewhat more fully upon certain points of discussion which had before been only incidentally touched upon.

The freshly expressed *muscular juice* is generally of a whitish colour, and turbid or opalescent from the presence of suspended fat; it reddens litmus paper very strongly, and forms on boiling a considerable coagulum; acetic acid, moreover, gives rise to a turbidity, which depends upon the presence of casein in the fluid, as I have satisfied myself by the application of rennet, &c. As the true muscular juice cannot of course be obtained without the admixture of the transudation entering into the connective tissue, and of the blood contained in the vessels of the muscular substance, a very great part of the albumen may be derived from this source; but the amount present is too large to be referrible to this only, more especially as we have met with it in considerable abundance in comparatively non-vascular tissues provided with smooth muscles, as, for instance, in the middle coat of the arteries. The casein must, however, be derived solely from the true muscular juice, since, as we have already shown in vol. i, p. 381, its presence cannot be demonstrated with certainty in the blood. We have already spoken at length, in vol. i, pp. 136, 141, 222, and 98, of the occurrence of *creatine*, *creatinine*, *inosic acid*, and *lactic acid*, in the muscular juice.

Scherer* has discovered a special substance in the decoction of the flesh of the heart of the ox, to which he has applied the term *inosite*. [See note to vol. i, p. 281 (on *inosite*) in the Appendix. —G. E. D.]

* Ann. d. Ch. u. Pharm. Bd. 73, S. 328-334.

Scherer* has also described several volatile acids, belonging to the group $C_nH_{n-1}O_3+HO$, which he found in the muscular juice; amongst these, acetic and formic acids were conspicuous.

It has generally been assumed that the muscles derived their colour from the quantity of blood contained in them; but we incline rather to Kölliker's† view, that there is a special colouring matter in the muscles. This pigment is very similar to that of the blood. It assumes a brighter red tint in the air, and is rendered darker by sulphuretted hydrogen; it may be extracted by water, and coagulates with the albumen of the muscular juice. These properties might dispose the chemist to regard the pigment of the muscle as identical with the colouring matter of the blood; but certain physiological grounds indicate that this pigment is not contained in vessels and blood-corpuscles, but adheres in a free state to the fibrils; the muscles retain their colour during vital contraction; colourless muscles are frequently as rich in blood-vessels as those which are strongly coloured; and a yellow colour may sometimes even be distinctly detected under the microscope in particular bundles.

The inorganic constituents are of considerable importance in the muscular juice, as well as in every other fluid; and we are indebted to Liebig‡ for the light which he has thrown on this subject by his carefully conducted observations. The inorganic, like the organic substances, must be regarded as something beyond mere incidental constituents of the muscular juice. This fluid, like most acid fluids, is rich in *potash salts* and *phosphates*, but poor in salts of soda and chlorides. It would appear, from numerous determinations of Liebig, that the relation of potash to soda in the blood of certain animals, on the one hand, and in the muscular juice of the same animals on the other, is about as follows: in the ash of both fluids there occur, for 100 parts of soda,

In the hen		40·8	of potash in the blood,	and	381	in the muscular juice.
„	ox	5·9	„	„	279	„
„	horse	9·5	„	„	285	„
„	fox	—	„	„	214	„
„	pike	—	„	„	497	„

It must be borne in mind that the muscular juice can never be

* Ann. d. Ch. u. Pharm. Bd. 69, S. 196–201.

† Mikrosk. Anat. Bd. 2, S. 248.

‡ Researches on the Chemistry of Food. Edited by William Gregory, M.D., Professor of Chemistry in the University of Edinburgh. London, 1847.

obtained free from blood and transudations, and that, consequently, the proportion of soda in the muscular juice would be even smaller if we could in any way exclude the admixture of blood.

A similar consideration presents itself to our notice when we proceed to estimate the quantity of *phosphoric acid* in the muscular juice. R. Weber* found from 45 to 47% of phosphoric acid in the ash of horses' flesh, and about 2% in that of the serum of the blood of the same animal. The phosphoric acid in the muscular juice is principally combined with potash, and only slightly with lime and magnesia. Chevreul found that the ash, yielded by a decoction of flesh, contained 81% of salts soluble in water, and R. Weber has more recently estimated their amount at from 79 to 80%. Liebig found in the ash of the muscular juice of oxen, horses, foxes, and deer, bibasic and tribasic alkaline phosphates, and in that of hens a small quantity of monobasic alkaline phosphate, in addition to the bibasic. The ash contains, therefore, in every case, more phosphoric acid than is required for the formation of the neutral phosphates of the alkalies. The conclusion to which we are led, that the muscular juice, when fresh, contains acid phosphates of the alkalies, gains confirmation from the fact that a large quantity of free lactic acid is contained in the fresh juice. We shall consider more fully, under the head of the "Metamorphoses of Animal Matter," the interesting views advanced by Liebig in connection with these relations.

R. Weber never found more than 7% of *chloride of sodium* in the ash of the muscular juice of the horse, but nearly as much as 73% in that of the blood-serum of the same animal.

The *alkaline sulphates* occur only in mere traces in the muscular fluid, and Liebig refers these salts to the admixture of blood.

Whilst the *phosphate of lime* is present in the blood in far larger quantities than the *phosphate of magnesia*, the reverse holds good in the muscular juice; in the muscular juice of the hen, for instance, according to Liebig, the ratio between these salts of lime and magnesia is as 10 : 39·2; and R. Weber found a similar ratio in the ash of horses' flesh.

Schlossberger† and von Bibra,‡ who have made comparative analyses of the flesh of different animals, have obtained the same results as Berzelius and Liebig for the amount of *muscular fibre*

* Pogg. Ann. Bd. 74, S. 91-115.

† Ann. d. Ch. u. Pharm. Bd. 72, S. 116-120.

‡ Arch. f. phys. Heilk. Bd. 4, S. 536-577.

in the flesh of mammals and birds, viz., from 15·8 to 16·7%; in the case of young animals, the numbers were somewhat less; in the flesh of reptiles and fishes, they were from 9·4 to 13·2%.

The substance of the vessels and nerves, as well as the nuclear fibres of the connective tissue and the sarcolemma, are naturally mixed with the muscular fibre in these determinations.

The question here arises whether we may, or may not, regard the protein-substance extracted from the flesh by means of water containing hydrochloric acid, as true muscular fibre; that is to say, as the cylindrical muscular bundles which are enclosed in the sarcolemma. According to Liebig,* this solvent extracts very different quantities of this protein-substance from the flesh of different animals; thus, for instance, the muscular fibres of the ox and the hen are almost entirely dissolved; a greater amount of substance remains from the flesh of sheep, and far more than half in the case of calves' flesh. We have already seen that by treating the flesh with acidified water the sarcolemma is perfectly emptied, with the exception of nuclei and granules, and a few small clots; hence, as Liebig's experiments are perfectly correct (as any one may ascertain by repeating them), it follows that calves' flesh contains relatively less fibre-substance (syntonin), and relatively more connective tissue, than the other kinds of flesh which were examined; as, for instance, that of oxen. This observation is further corroborated by a simple microscopical comparison of the primitive bundles of muscle in the ox and the calf. Donders† noticed the striking difference of diameter in the primitive bundles of the cow and the calf, and he is of opinion that the number of the bundles remains the same during the growth of the calf; in which case, the fibre-substance (syntonin) would alone increase during the growth of the animal, whilst the sarcolemma and connective tissue remained the same. It may be assumed that the diameter of the primitive bundles of the calf is from $\frac{1}{4}$ to $\frac{3}{8}$ smaller than that of the primitive bundles of the full-grown ox. If the number of the bundles remains the same, and if the sarcolemma and connective tissue do not increase with the growth of the muscle, it becomes a mathematical necessity that less muscle-fibrin (syntonin) admits of being extracted from the flesh of calves than from that of oxen. There can be no doubt, from the micro-chemical reactions already indicated, that the protein-substance which can be extracted by

* Ann. d. Ch. u. Pharm. Bd. 75, S. 126.

† Mulder's Vers. einer physiol. Chem. S. 630, Anm. [or English Transl. p. 578, note.]

dilute hydrochloric acid constitutes the essential part of the muscular fibrils, and is perfectly identical with the substance of the smooth muscular fibres of other contractile tissues.

The ratio which the sarcolemma bears to the enclosed cylinder of muscular fibre has never been even approximately determined. The usual method of determining the connective tissue contained in the muscles is by ascertaining the quantity of gelatin yielded by boiling the previously rinsed muscle, but this can only be regarded as a very rough mode of determination. Liebig gives 5·6% as the mean quantity of gelatigenous substance in flesh; von Bibra found about 2% in the majority of the different kinds of flesh which he examined.

If we take the gelatin that is formed as a measure of the quantity of connective tissue contained in the muscles, we must bear in mind that, on boiling with water, the nuclear fibres (which, it would appear from micro-chemical investigations, are present in considerable quantities in the muscles) remain undissolved, whilst the protein substance, in quantities varying according to the duration of the boiling, becomes dissolved with the gelatin (Mulder's tritoxide of protein).

Liebig estimates the *constituents* of ox-flesh which are *soluble* in water at 6%, of which 2·96% are *albumen.* This result agrees with the analyses of Berzelius, Braconnot, Schütz, Schlossberger, and von Bibra. In the flesh of birds the quantity of soluble substances amounts to as much as 8%, as is shown by the analyses of Schlossberger and von Bibra.

Fat is always to be found in flesh, notwithstanding the most careful preparation of the muscle, being derived not only from fat-cells, but from the blood, the nerves, and even from the muscular substance itself, in the fibrils of which we frequently observe fat-globules amongst the nuclei. Liebig always found 2% in the flesh of the ox, von Bibra found even as much as 4·24% in that of a man aged fifty-nine years, but only about 2% in that of other mammals, whilst he could not discover more than about from 0·54 to 1·11% in the muscle of fishes.

The quantity of *water* in the muscles, when in a fresh state, was estimated by Berzelius* at 77·17%, by Schlossberger† at 77·5%, and by Schütz‡ at 77·6%, in the ox; von Bibra found from 72·56

* Lehrb. de Chem. Bd. 9, S. 588.

† Untersuch. über d. Fleisch verschiedner Thiere.

‡ Vergleichende chem. Untersuchungen des Fleisches verschiedner Thiere. 1841.

to 74·45% in human muscles. These and similar determinations, which have been instituted as to the muscles of different animals, are not devoid of significance; but as they vary even in the same species of animals, they cannot attain any high degree of importance until they can be compared with the quantity of water contained in the blood, or, better still, with that in the blood-serum. Thus, for instance, it would be highly important in reference to the mechanical metamorphosis of matter, to ascertain the proportions existing between the water contained in the muscles and that in the blood under different physiological and pathological conditions. A course of experiments, bearing on this subject, has lately been instituted by one of my pupils. It was found that, on an average, there are 9·9% less of water in the muscle than in the serum of the blood, and that this proportion continues nearly the same whether the blood was in a concentrated state or contained an excess of water. This proposition, which is precisely what might have been anticipated, was found to be fully confirmed in comparative analyses of the blood and muscle of persons who had died from cholera, as well as in so-called hydræmic conditions. We may, unquestionably, expect the most important results regarding the mechanical metamorphosis of animal matter from investigations into the proportions existing between the quantity of water contained in the blood and the other juices, tissues, and organs of the animal body, under different conditions.

It will be readily understood that the determination of the quantity of water contained in the muscles should be conducted with the utmost care, as pieces of muscle very rapidly lose a certain quantity of water when exposed to the air, and thus afford only a very inexact result. Great care must be taken to avoid any evaporation from the portion of muscle which is to be weighed. Another circumstance which calls for attention is, that while the surface of the piece of muscle, when placed in an air-bath or in a vacuum, dries very rapidly, the interior obstinately retains its water. It should moreover, be borne in mind, that it is not always easy to obtain a portion of muscle alike poor in connective tissue and vessels, and that the amount of connective tissue essentially influences the quantity of water. In examining the muscular substance of the human subject, the observation is rendered very much more difficult, from the circumstance that dissection must necessarily be postponed till eight or even fifteen hours after death, when endosmotic currents may have been already established in the muscular sub-

stance as well as in the blood, which do not affect the distribution of the water in the living body.

The serum of the blood obtained from the dead body was not found by these observations to differ in its amount of water from the blood drawn by venesection during life; but, on an average, a larger amount of water than that given by any former observers was found in the muscles (upwards of 80$\frac{0}{0}$ in the bodies of healthy persons who had committed suicide); it must remain undecided for the present whether this excess of water depends upon an absorption of the fluid by the muscles after death, or whether a more careful mode of determining its amount may have yielded a higher number for the water, and thus afforded a more correct result.

Both for the purpose of giving a general view of the subject, and in order to furnish certain definite points of support for the establishment of future observations on the metamorphosis of animal mater, we here subjoin a list of the mean results of former determinations of the individual constituents of the muscular substance; we limit ourselves more especially to the flesh of oxen:—

	Per cent.		Per cent.
Water	74·0	to	80·0
Solid constituents	26·0	„	20·0
	100·0		100·0
Muscular fibre	15·4	„	17·7
Gelatigenous substance	0·6	„	1·9
Albumen	2·2	„	3·0
Creatine	0·07	„	0·14
Creatinine	undetermined.		
Inosic acid	ditto		
Fat	1·5	to	2·30
Lactic acid ($C_6H_5O_5$. HO)	0·60	„	0·68
Phosphoric acid	0·66	„	0·70
Potash	0·50	„	0·54
Soda	0·07	„	0·09
Chloride of sodium	0·04	„	0·09
Lime	0·02	„	0·03
Magnesia	0·04	„	0·05

It would scarcely appear necessary to enter more particularly into the consideration of the methods to be employed in the *chemical investigation* of the animal muscles, as the remarks already made in reference to the analysis of the organic muscles apply equally

to the animal muscles; we must, however, offer a few remarks on certain points to which we have not been previously able to allude. We refer especially to the examination of the fluid contained in the sarcolemma, and permeating the muscular bundles. We are, unfortunately, unable to procure this fluid free from the *liquor sanguinis*, and hence we know of no better method to recommend than that adopted by Liebig. It is self-evident that the muscle selected for examination should be fresh, and freed, as far as possible, by means of the scalpel from fat, tendon, membranes, cellular tissue, vessels, and nerves; it should then be finely minced, chopped, or shredded, taking care that no splinters of wood or other extraneous substances are mixed with the object. According to Liebig's directions, half of the chopped flesh should be put into an equal weight of water, and after being duly kneaded into a pulpy mass, should be exposed to pressure in a linen strainer. The residue, after pressure, must be again twice kneaded with water and pressed, so that we obtain three extracts from the first half of the flesh. The fluid of the second pressing of this first half is employed for the first extraction of the second half of the reserved chopped flesh; whilst the fluid of the third pressing is used for a second extraction of the second portion, which is then again extracted with pure water. The flesh of fishes and certain amphibia cannot be submitted to pressure in a finely chopped state, as it swells in water into a thick gelatinous mass, which clogs up the pores of the linen. According to Liebig, we must here have recourse to the process of displacement. The muscular substance of frogs differs from that of fishes; it admits very readily of being pressed, and is, therefore, peculiarly well adapted for experiments of this nature.

The expressed acid fluid, which is either turbid, or at all events opalescent from the presence of fat, must be treated in the water-bath until all the coagulable matters separate from the solution. The expressed fluid, after the removal of the coagula by filtration, is either of a faint reddish hue, or nearly colourless. The evaporation requires to be conducted with extreme caution, and Liebig has drawn attention to the circumstance that the fluid is disposed to assume a brownish colour during the process of evaporation, in consequence of the presence of the free acid. On this account Liebig recommends the addition of baryta water, so long as any precipitate is deposited, not only for the purpose of neutralising the fluid, but also that the phosphates may be removed as far as possible. The next step is to crystallize the greater part of the creatine contained in the fluid, according to the method indicated in vol. i,

p. 135, and this being done, the inosic acid must be separated in the manner described in vol. i, p. 222, viz. :—by adding alcohol to the mother-liquid of the creatine. About 5 times the volume of spirit should then be added to the mother-liquid of the inosates of potash and baryta, on which the fluid separates into two layers, the upper one of which contains lactate, acetate and butyrate of potash and creatinine. In order to separate the latter substance, we treat this lighter fluid with ether, on which it again separates into two layers, the upper one of which contains nearly pure creatinine, which crystallises on the evaporation of the ether. The lactic acid and the above-described volatile acids of the heavier layer are separated according to the usual methods. In the heavier stratum of the mother-liquid of the inosates which is formed by the action of the spirit, the main contents, in addition to the extractive matters, are inosite and chloride of potassium. It is easy to obtain evidence of the presence of creatinine in fresh muscular juice by Liebig's method of boiling the solid residue of the mother-liquid of the inosates in spirit of wine, and adding chloride of zinc to the spirituous fluid, which causes the compound of chloride of zinc and creatine to separate in a crystalline form.

The examination of the parts which are insoluble in water does not call for any additional remarks, as it has been already noticed in detail in the preceding pages; in general, however, the mode of investigation corresponds with that which has been described for the organic muscles.

If we inquire whether the chemical investigations of the muscular substance which have been hitherto made, throw any light on the nature of its functions, we find that very little information has been gained which can either afford support to any of the existing hypotheses, or can suggest new ones. By proceeding with the greatest caution by the method of induction, we arrive at the following conclusion :—

The protein-substance, which can be extracted from the muscular fibrils by extremely dilute hydrochloric acid, is the most essential element of animal motion ; it is one and the same in the striped muscular fibres, in the smooth muscles, and in the tissues which were formerly termed contractile. It is, however, peculiar to those organs whose movements are dependent on the nervous system. We are unable to explain on chemical grounds the manner in which this substance alters its physical properties during the contractions of the tissues.

The voluntary and involuntary muscles contain moreover a

fluid surrounding and permeating the above-described matrix of the contractile fibres, which is distinguished by its acidity, and differs entirely from the plasma of the blood. Liebig has calculated that the voluntary muscles alone contain more than sufficient free acid completely to destroy the alkalinity of the blood. We have already seen that wherever contractile fibres or fibre-cells are present, the potash-salts and phosphates predominate in this fluid, whilst the blood-plasma, on the contrary, is poor in these salts, but rich in alkaline chlorides and soda-salts. The difference thus observable in the intercellular fluid of the blood-cells and that of the contractile fibres cannot be merely accidental; and Liebig has suggested that it very probably either occasions, or is occasioned by an electrical current. We know, however, that Du Bois Reymond * has subsequently arrived at many novel views, and obtained some brilliant results relating to the electrical phenomena of muscular contraction, in repeating the observations of Matteucci. The existence of an intimate connection between the development of electricity accompanying muscular contractions and the acid of the muscular juice on the one hand, and the alkali of the blood on the other, and the importance of the chemical constitution of the muscular juice on the function of the organ, are corroborated by the striking and well-known fact, that all muscles, whether voluntary or involuntary (both the striped and the smooth) lose their contractility very rapidly in water. (Lukewarm water at $+37^\circ$ scarcely acts less rapidly on this property of muscles than cold water.) The experiment of the younger Liebig† seems opposed to this observation, which may be tested by any one who watches by means of a rotatory apparatus the contraction of the transversely striated muscles of a recently killed animal, or its stomach, intestinal canal, bladder, &c. This observer found that muscles, which had been freed as thoroughly as possible from blood by the injection of water into the vessels, retained their contractile property as long as those muscles which still contained blood. These two observations do not, however, involve a contradiction; for if the muscles do not lose their contractility in the absence of blood, but do so on the addition of water, it simply shows that the muscle loses its capacity for contraction by the dilution of the muscular juice. If, therefore, we connect the development of electricity during muscular contraction with chemical forces, we shall find that the causes of the phenomena of polarity

* Unters. üb. thier. Elektricität. Berl. 1848 u. 1849.

† Ber. der Akad. d. Wissensch. zu Berlin, 1850, S. 339-347.

depend less upon the antagonism of alkali and acid than on that of the solid muscular fibrils (syntonin) and the muscular juice.

Although we purpose at a future page reverting to the interesting observations of the younger Liebig, we cannot abstain from making a few remarks in relation to them in the present place. It would appear from these experiments that muscle is dependent on oxygen to enable it to contract; for Liebig found that frogs' muscles retained their contractility much longer in an atmosphere of oxygen than in air which did not contain oxygen, as, for instance, in carbonic acid, nitrogen, or hydrogen. It was further shown by two carefully conducted experiments that, whilst the muscle is in a state of contraction, oxygen is absorbed, and a corresponding quantity of carbonic acid is exhaled,—facts which confirm the previously advanced proposition, that a large portion of the carbonic acid formed in the animal body is generated not in the capillaries, but in the parenchyma of the organs, and is especially produced by muscular action. We need scarcely remark that the results of these observations are of the highest importance in relation to the theory of metamorphosis of matter, whilst they afford powerful support to the purely physical hypothesis of the elder Liebig in relation to this subject.

Nerves and Brain.

The nervous system and the brain contain nerve-fibres and nerve-cells as their special and peculiar morphological constituents.

The *nerve-fibres* or tubes which are distributed throughout the peripheral nerves, the spinal cord, the brain, and the ganglia, do not all present the same appearance, when seen under the microscope; hence the nerve-fibres have been divided into two kinds, namely, the thicker (animal, cerebro-spinal), and the more delicate (sympathetic, vegetative, organic); there is no ramification observable in either of these classes of fibres, except at their extreme terminations.

The thicker nerve-fibres form cylindrical filaments, varying from 0·004 to 0·010‴ in diameter; they occur especially in the nerves springing from the spinal cord, but they are also met with in other parts of the nervous system. When these nerve-fibres are examined under the microscope in a perfectly fresh state, especially after the addition of a little albumen, they appear

entirely homogeneous and transparent, exhibiting a sharply defined contour. But after lying for some time or having come in contact with water, they exhibit a double contour, resembling broad dark bands, with a clear stripe running down the middle. This peculiarity, together with the size of their diameter, especially distinguishes them from the so-called sympathetic fibres. Distinct morphological elements may be recognised in each of these fibres; and, in the first place, we must distinguish between the coat or sheath and the contents.

The coat or limitary membrane of the nerve-tubes can scarcely be recognised in very recent nerves, for this membrane is an entirely structureless, transparent, somewhat elastic membrane, which can only be rendered visible by the application of certain chemical reagents which we shall presently mention.

The substance contained in the nerve-tubes (the nerve-medulla or pulp) appear at first, as we have already observed, to be perfectly homogeneous, whence it has been assumed by many observers to be an entirely homogeneous, closely mixed matter. It is quite immaterial to our purpose, whether we admit the correctness of this view, or adopt the opinion held by others, that the subsequently visible separation of the medulla into a cortical substance and a cylindrical axis-fibre, exists pre-formed in fresh nerves; but, judging from a chemical point of view, we are compelled to assume the most decided morphological separation. Thus, the application of cold, or the addition of water, or of certain chemical agents, gives rise to a kind of coagulation in the medulla, causing the outermost layer of the contents of the nerve-tubes to become darker, somewhat grumous, or even granular; whilst in the interior, that is to say, in the long axis of the nerve-fibre, there remains a clear, somewhat sharply defined filiform stripe—the central or axis-fibre, or axis-cylinder. The actual medullary substance, or nerve-pulp, assumes very different forms when subjected to rough pressure, appearing in different cases in nodular, cylindrical, or clavate shapes as it protrudes from the sheath. Within the tubes the substance is frequently accumulated in an irregular manner, distending the sheath unequally at different points, which gives rise to those varicose nerve-fibres which we so frequently meet with in examining the brain.

The finer or sympathetic nerve-fibres have a diameter varying between 0·00212 and 0·00300'''. These fibres bear less resemblance to tubes than to solid cylinders, and have generally no trace of any contents. They occur principally in the sympathetic,

forming bundles of a somewhat bluish grey colour, whilst the cerebro-spinal fibres appear white and of a silvery lustre. They are, however, found interspersed in various quantities in all other nerves, more especially in those of the involuntary muscles, the skin, and the mucous membranes (Bidder and Volkmann*), and lastly in the posterior roots of the spinal nerves and in those of the sensitive cranial nerves (Kölliker)†. It is only in the peripheral extremities of the cerebro-spinal nerves that the animal fibres become so attenuated that they resemble in their diameter and general appearance the above-described sympathetic fibres. These nerve-fibres are also inclosed in a sheath, which cannot always be distinctly recognised, even after the application of chemical reagents; on the other hand, the axis-cylinder may be very easily brought into view in these nerves by chemical means, which we shall notice more particularly in a future page.

Nerve-fibres containing no medulla have been detected by R. Wagner, Remak, Bowman, Kölliker, and other histologists, in the pale fibres of the Pacinian corpuscles, in the extremities of the olfactory nerves, in the nerves of the cornea, in the electrical organ of the Torpedo and Ray (where there is an actual ramification of the fibres), and in the extremities of the nerves of the skin of the mouse. These fibres appear from the observations hitherto made in relation to this subject, to consist only of a sheath and an axis-cylinder.

Another class of nervous fibres has been assumed to exist, namely, Remak's fibres, in which nuclei may be detected, more especially after the addition of acetic acid; but it has not yet been decided whether these elements which have been observed in the ganglia of the sympathetic, &c., are true nerve-fibres, or merely a peculiar form of connective tissue.

Larger or smaller bundles of nerve-fibres are surrounded by a fibrous, strongly glistening, white, dense membrane, called the neurolemma. It appears on a closer examination to consist of different forms of connective tissue, with which are interspersed numerous elastic fibres.

The Pacinian bodies form a very singular appendage to the nerve-fibres. These bodies, which are present in very large numbers in the hands and feet of man and many carnivorous animals, and in the mesentery of the cat, are oval, consist (somewhat like onions)

* Die Selbstständigkeit des sympathischen Nervensystems. Leipzig, 1842.

† Selbstständigkeit und Abhängigkeit des sympathischen Nervensystems. Zürich, 1844.

of nearly concentric membranes, measure from 0·5 to 2·0‴, and a nerve-fibre terminates in each of them. These concentric membranes are composed of connective tissue, and between the coats there is a serous fluid, which collects in larger quantities in the narrow, long, central space of these Pacinian bodies. Each of these corpuscles is attached to the nerve to which it belongs by means of a short pedicle, which is formed by layers of the connective tissue of the bodies, and by the neurolemma; through this pedicle an animal nerve-fibre proceeds from the nerve, and extending to the central cavity of the corpuscle, diminishes rapidly until it resembles the axis-cylinder. It traverses the narrow central space, and, after splitting into two or three parts, terminates opposite its point of entrance in fine nodules.

In the nervous system, and more especially in the central organs, as the brain, the spinal cord, and the ganglia of the spinal nerves and of the sympathetic, there occur, in addition to the fibres, peculiar cells, termed the nerve-cells, (accessory corpuscles, or ganglionic globules). These bodies are true cells, consisting of an investing membrane, a nucleus with one or more nucleoli, and soft contents interspersed with molecular granules. The size of these nerve-cells is as various as the diameter of the nerve-tubes, and they may be divided into large and small, as we divide the nerve-tubes into thick and thin. The smaller nerve-cells occur principally in the ganglia of the sympathetic, and the larger ones in company with the double-outlined fibres of the cerebro-spinal nervous system; but this rule is not without many exceptions. The diameter of the larger nerve-cells is about 0·05 or 0·06‴, whilst that of the smaller cells is frequently not more than 0·002 or 0·003‴ (Kölliker).

These cells vary in form no less than in size. Large, almost spherical or oval cells occur principally in the grey substance of the brain and spinal cord. Fusiform, trapezoidal, irregularly triangular nerve-cells, provided with numerous, and often ramifying processes, abound in the grey substance of the central organs. We find in the ganglia of the sympathetic scarcely any cells which have not one or two pale processes. Many of the nerve-fibres take their origin from these cells, and we often see one, and not unfrequently two fibres proceeding from a single cell.

The nerve-cells are covered externally by a structureless membrane, which is in some cases extremely thin and scarcely visible, and in others somewhat thicker and easy of recognition. The cells which have thin walls occur more especially in the central

organs, whilst those having thicker walls are almost limited to the ganglia. The investing membrane of the latter is very elastic, so that the cells, without being lacerated, admit of being compressed and expanded, resuming their former shape when the pressure is removed. The processes, like the axis-fibres, are remarkable for their elasticity (R. Wagner, Kölliker).

The nuclei, which generally occupy the centre of the cells, are for the most part spherical or oval, have sharply defined outlines, and contain clear fat-like matters, amongst which one, or even two roundish or elongated nucleoli may in general be distinguished. The size of the nuclei varies from 0·0015 to 0·008‴, whilst the nucleoli measure from 0·0005 to 0·0003‴ (Kölliker).

In addition to the nuclei the nerve-cells contain a tough, semi-fluid mass, which is either colourless, or of a faint yellow hue, and holds in suspension finer or coarser granules. In some cases, and more especially in the stellate* cells of the spinal cord, this dark granular mass is collected into various groups or masses, whilst other portions of the cells appear to be less granular.

We see from this short description of the morphological constituents of the nervous system, that we have to take into consideration in the chemical investigation of the nervous mass numerous substances, whose difference is made apparent by their variety of form. We will now consider somewhat more minutely the alterations effected on the above-described morphological elements by the action of various chemical reagents, and then endeavour to give a more general representation of the chemical constitution of nervous matter.

We have already observed that pure *water* effects a change on fresh nerves which have been removed from animals immediately after they had been killed. The contents of the nerve-tubes pass into a state resembling that of coagulation, which causes the double contour of the cerebro-spinal nerves to appear more distinct, and a coarsely granular mass to separate itself from the periphery towards the centre, whilst in the centre itself there remains an irregularly twisted intestine-like stripe of a light or pale reddish colour. The nerve-cells are scarcely altered by the action of water, or, at all events, no alteration can be definitely recognised in any part of the cell. (*F.* P. 15, F. 5.)

Cold *alcohol*, since it abstracts water from the nervous and cerebral matter, renders these parts harder and almost brittle, but it

* [The terms *caudate* and *stellate* have been applied to these cells, according as they have one or se veral of the processes or prolongations.—G. E. D.]

gives rise to very few visible alterations in the microscopical characters of the nervous substance. Hot, or more correctly speaking, boiling alcohol behaves differently; for, as we might assume *à priori,* it coagulates the coagulable parts of the nerves, and dissolves the fat and the salts of the fatty acids. When the nerve-fibres are boiled in alcohol the nerve-sheath exhibits a sharper outline, appearing at different points as a special membrane, distinct from the granular contents. The contents have the appearance of less dark and less well defined granules, and are generally translucent and somewhat faintly defined. The axis-cylinder often stands out very well in some fibres, although a careful preparation and some minutes' boiling are necessary to exhibit this clearly. The nerve-cells are but slightly altered by boiling with alcohol, the change they undergo being for the most part limited to an appearance of slighter granulation. The alcohol in which the nervous matter has been boiled exhibits on cooling white flakes, which appear, when seen under the microscope, to be neither crystalline nor of the nodular form common to the fat of the nerves, but to consist of a confused mass of fine molecular granules. (*F.* P. 15, F. 6.)

Cold and hot *ether* behave towards the nervous elements in much the same manner as alcohol, and like the latter, render large pieces of nervous substance somewhat harder. When examined under the microscope the double contour of the cerebro-spinal nerves is found to disappear under the prolonged action of ether, whilst the sheath appears more distinct at certain points, and studded, as it were, with granules in many parts. The granular contents are rendered considerably paler, whilst here and there the axis-cylinder is seen paler, and like a twisted thread. The action of ether on the nerve-cells is as slight as that of alcohol. The ether in which the nerve-fibres have been digested deposites on evaporation white granules, which appear, when seen under the microscope, to consist of crystals of margaric acid and nodular masses of brain fat.

Dilute *acetic acid* produces no marked alteration in the morphological character of the nerve-tubes, but when this acid is used in a highly concentrated state, the nerve-fibres after its prolonged action acquire a sharply defined outline. Although the inner contour becomes somewhat distorted after boiling, the sheath becomes distinctly visible at certain points on the cut surfaces of the nerve-fibres; between the inner contours there remains a coiled, often pale reddish stripe; thin, very pale threads frequently

project from the extremities of the torn nerve-fibres; they can often be traced for some distance along the uninjured nerve-tube, and are unquestionably axis-cylinders. Kölliker has noticed the difficulty and slowness with which these filaments dissolve even on being boiled with concentrated acetic acid. When concentrated acetic acid is added to a nerve-fibre whilst under the microscope, the nerve is seen to retract instantaneously, whilst the granular nerve-pulp and very pale fibres, which are evidently the axis-cylinder, project from the cut ends (Kölliker). The fine nerve-fibres of the sympathetic system also swell in acetic acid, their contents become grumous, whilst at different spots an axis-cylinder becomes visible under favourable circumstances. Besides these fibres we may frequently discover the pale nucleated fibres of Remak; we must, however, be careful not to confound them with the fibres of connective tissue, which also exhibit many narrow nuclei in the cerebro-spinal nerves on the addition of acetic acid. (*F.* P. 15, F. 6.)

It will be found that the behaviour of the nerve-cells towards acetic acid precisely accords with the account given by Kölliker. The individual parts of the cell generally become somewhat more visible in dilute acid; the cell-membrane exhibits a more distinct contour, the contents of the cells become more granular and often more turbid, but notwithstanding this the nucleus not unfrequently appears distinctly visible. Concentrated acetic acid, after prolonged action or on the application of heat, causes the cell-membranes to swell till at length they become wholly invisible. The granular contents are dissolved, with the exception of the darker granules, which occur in some of the cells; and even the nuclei, which at first come more distinctly into view, finally disappear.

Very dilute *hydrochloric acid* (1 part in 12,560 parts of water) causes the nerve-fibre to swell, and renders the contents far more transparent. The separate fibres exhibit beautiful, sharply defined double contours; between which there remains in the middle a perfectly transparent, tolerably broad space, which appears almost empty. Neither nerve-sheath nor axis-cylinder can anywhere be distinctly recognised. The delicate fibres of the sympathetic are not visibly altered in this very dilute solution of the acid, but the nuclei of Remak's fibres, as well as those of the connective tissue, are brought more prominently to view.

There is very little alteration perceptible in the nerve-cells, even after a very prolonged action of this solution of the acid;

at most the membrane is rendered somewhat more hyaline and the contents rather more grumous.

Concentrated hydrochloric acid does not bring into view the individual morphological elements either in the fibres or the cells; but converts the whole into a pultaceous mass of smaller or larger strongly granulated dark clots, which, although most commonly roundish, may assume the most varied and capricious forms. If any remains of nerve-fibres are present, they are found to be very much thickened; the dark clots are perfectly isolated and arranged only in one direction, and no trace of a nerve-sheath is perceptible. When a freshly prepared microscopical preparation is treated with concentrated hydrochloric acid, the individual nerve-fibres diminish in length, but increase to an extraordinary degree in breadth; the nerve-pulp becomes coarsely granular and dark, whilst from the cut extremities nodular or coarsely granular masses protrude, and most distinctly bring into view the coiled roundish threads or axis-cylinders. In this way more frequently than by any other method of exhibiting the axis-cylinder, I have been able to see the sheath and nerve-pulp dissolve in the middle of a fibre, leaving only the axis-cylinder, which at these points might be traced in both directions through the comparatively uninjured nerve-fibre. The peculiar property of concentrated hydrochloric acid in simultaneously thickening and shortening the nerve-fibre is beautifully illustrated in small bundles of nervous fibres, which are surrounded by the neurolemma. The latter varies in expansibility according to the amount of connective or elastic fibres which it contains. When, therefore, the nerve-tubes which it encloses are much swollen, several protuberant dilatations and corresponding constrictions appear in one and the same bundle. The fibres projecting from the neurolemma at the extremities of the bundles diverge in a brush-like form, whilst the nerve-pulp protrudes from the cut extremities of the fibres, giving to the whole a bouquet-like appearance.

When fresh nerve-fibres are allowed to remain for some time immersed in concentrated *nitric acid*, the whole mass becomes intensely yellow and very friable or soft. On observing under the microscope the direct action of nitric acid, we find that the individual fibres are thickened and shortened as in the case of concentrated hydrochloric acid, although in a less degree. The double contours cease to be recognisable in fibres which have been treated for a longer period with nitric acid; the whole contents of the nerves appear coarsely granulated, and we can perceive no light

interspace, or bright central stripe: the nerve-tubes are generally found to have become thinner rather than thicker, and the nerve-sheath can scarcely be recognised with certainty. It is seldom, however, that a microscopical preparation of this kind is thoroughly examined without our detecting some nerve-fibres with the axis-cylinder most distinctly projecting from one extremity like the wick from a taper. Frequently, indeed, six or more of these taper-like nerve-tubes may be seen, the projecting axis-cylinders of which exhibit a distinct yellow colour; these have frequently an undulating outline when they project to any great distance, and in some rarer cases have an intestine-like coiled appearance. If fibres, which have been treated with nitric aid, are boiled with absolute alcohol, they become very hyaline, and their outlines grow less distinct, although the yellow transparent nerve-sheath may still be detected at different spots, whilst the interior exhibits a faint granulation, the colour of which cannot, however, be determined with certainty. The axis-cylinders are often thus seen more distinctly than by the mere application of nitric acid. (*F.* P. 15, F. 6.)

If we boil teased (or unravelled) nerves with alcohol and ether, and after the removal of these fluids allow them to remain for some time in concentrated nitric acid, the nerve-sheath, as Kölliker has already observed, is brought into view, exhibiting faint granules and very beautiful, often detached axis-cylinders. Under favourable conditions there is scarcely any means by which the sheath and axis-cylinder can be more beautifully exhibited.

The first effect of concentrated nitric acid upon the nerve-cells is to render the cell-walls more distinct, and the contents more granular; the cell-membrane, however, soon disappears, and we can perceive only the nucleus in addition to a confluent granular pulpy mass. When the grey substance of the brain has been immersed for any length of time in concentrated nitric acid, nothing can be recognised in addition to the elements of the fibres, excepting nuclei and nucleoli, which are the sole remnants of the nerve-cells.

Concentrated *sulphuric acid* (the third hydrate) forms a fine purplish red or violet fluid, after remaining for some time in contact with the nerve-fibres. The colour resembles that which appears in Pettenkofer's bile-test. The addition of sugar is not necessary for the production of this colour. The separate nerve-fibres exhibit a very beautiful violet tint when seen under the microscope; the nerve-sheath, which is found to swell in a gelatinous manner when sulphuric acid is added to a fresh preparation, is rendered entirely invisible in this case. The nerve-pulp is converted into

an uncommonly fine granular indistinct body, and it is only in rare cases, although then with extreme distinctness, that the axis-cylinders can be recognised in the individual fragments of nerves. The fluid containing granules and viscid globules, and surrounding the partially undestroyed nerves, is likewise of a violet colour.

Chromic acid, or a saturated solution of the bichromate of potash, when decomposed with a little sulphuric acid, contracts the transverse diameter of the nerve-fibres, and imparts to them an intense yellow colour. After the nerve-fibres have been immersed for a considerable time in this fluid, they appear somewhat narrower, but sharply defined (the double contours of the animal nerve-fibres are, however, no longer visible); the nerve-pulp becomes more coarsely granular and renders the fibres opaque, so that the axis-cylinder can no longer be seen within them. The contracting action of this reagent on the sheath is very beautifully and distinctly shown; we observe at different spots irregular, nodular, but most commonly roundish drops of nerve-fat protruding from it. When the action of the chromic acid is not too strong, the sheath exhibits rents, from which the viscid nerve-pulp exudes, and this appearance is so clearly defined that it is impossible to refer it to any deception. The sheath is completely burst or destroyed at different points, and the nerve-pulp diffused through the fluid, so that nothing but the pale-coloured, sharply outlined filiform axis-cylinder remains visible, whilst in other nerve-tubes the transition of the cylinder into slightly altered fibres may be distinctly traced. With the exception of the following reagent there is nothing which exhibits the morphological constituents of the nerve-tubes more distinctly than chromic acid.

This acid causes the nerve-cells in some degree to contract, and generally renders their outlines more distinct. The contents are scarcely rendered more grumous than they previously were, whilst there is no important difference to be perceived either in the nucleus or the nucleolus. The cerebral and the ganglionic masses are moreover hardened by the action of chromic acid.

An *aqueous solution of iodine* (or what is better), iodine in a solution of hydriodic acid, colours the nerves yellow, and leaves the fibres tolerably coherent, so that they may be very easily prepared for microscopical investigation, and traced into the individual filaments. After the prolonged action of the above-named fluid each individual nerve-tube acquires a pale yellow appearance, and becomes broader, showing a tolerably distinct contour (the animal

fibres without double contours); the sheath can be readily recognised at individual points; the grumous, but very finely granular pulp appears to fill the whole cylinder, although by a proper mode of arrangement the axis-cylinder may be traced with the greatest distinctness within the nerve-fibre, following a straight rather than a coiled direction. If the preparation has been very thoroughly unravelled, the axis-cylinder may often be seen protruding from $\frac{1}{10}$th to $\frac{1}{8}$th of a line beyond one of the uninjured nerve-fibres, being generally straight or slightly bent, rounded, and of a faint yellow colour; but occasionally presenting a somewhat coiled appearance.

The aqueous solution of iodine acts upon the nerve-cells in nearly the same manner as upon the fibres.

Millon's reagent (subnitrate of mercury with nitrous acid) renders portions of nerve hard and tough, and gives them an intense purple colour. The individual bundles do not admit readily of being separated into fibres. Under the microscope the nerve-sheath exhibits a sharp outline; the pulp is not so coarsely granular as after the application of chromic acid, nor so delicate as after the action of hydriodic acid. The granules render the whole nerve-tube very dark, and prevent the recognition of the axis-cylinder. In preparations obtained by unravelling or teasing, we see, however, a number of axis-cylinders either isolated or projecting in a very twisted form from a portion of undestroyed nerve-fibre. The microscope scarcely shows any trace of colour in the individual nerve-fibres, or, at most exhibits only a yellowish, and not a violet colour.

A solution of corrosive sublimate, which is especially recommended by Purkinje for the exhibition of the axis-cylinder, acts independently of the coloration in very nearly the same manner as subnitrate of mercury; but the use of this reagent scarcely facilitates the detection of the axis-cylinder within the uninjured nerve-tube more than the preceding fluid.

The grey cerebral substance, and the sympathetic ganglia harden when immersed in solutions of these two metallic salts. The nerve-cells slightly shrivel, and the cell-membrane is rather more distinct: the contents become more grumous and untransparent, so that the nuclei cannot easily be detected, and the nucleoli only with great difficulty.

A very concentrated solution of *chloride of calcium* renders small nerve-bundles somewhat transparent, but at the same time extremely tough and elastic, so that it is only with great care that

we can obtain even a moderately good preparation, in consequence of the extreme difficulty of separating the fibres. When viewed under the microscope the isolated nerve-fibres appear coiled in an intestine-like manner and somewhat distended, the sheath cannot readily be distinguished, and the pulp is converted into a somewhat coarsely granular matter, showing no distinct central fibres; it is only at particular points that a portion of the axis-cylinder may be seen projecting from the extremity of a fibre like the wick from the end of a candle.

When immersed in a concentrated solution of *carbonate of potash*, the nerve-tubes swell somewhat up, and seem partially twisted, the nerve-sheath being unequally extended, so that the tube resembles the colon in form. The individual dilatations are not sharply separated from each other, but on the whole the contents are rather clear and translucent than granular; the axis-cylinder and sheath cannot be recognised. Some light roundish filaments may be seen at the extremities of individual nerve-fibres which bear an extraordinary resemblance to axis-cylinders, although it is not very certain that they may not be due to the connective tissue, which frequently gives rise to precisely similar filaments. In our description of the above experiments we have therefore only designated these filaments as axis-cylinders in those cases in which their form and position showed they could be nothing else. Objective certainty was unattainable in regard to these filaments, although it seems in the highest degree probable that the axis-cylinder remains uninjured in carbonate of potash.

Virchow* first noticed that the substance of the nerves becomes hardened in solutions of carbonate of potash; the fact, observed by my friend Ed. Weber, is especially worthy of notice, that the course of the fibres may be traced in an extremely beautiful manner in the brain and spinal cord, when they have been previously treated with a solution of this salt.

The nerve-cells are also but slightly altered in form in solutions of carbonate of potash.

If prepared nerves are suffered to be immersed for any length of time in a *dilute solution of soda*, the separate fibres appear to become more faintly granulated, somewhat contracted in their diameter, and no axis-cylinder can be detected; the double contours of the cerebro-spinal fibres are also no longer visible. But when a dilute solution of soda is added to a fresh preparation whilst under the microscope, the sheath contracts, as was observed by

* Zeitsch. f. rat. Med. Bd. 4, S. 276.

Kölliker; while the nerve-pulp protrudes either at the extremities of the torn fibres, or through the sheath, which bursts at the point of contraction, in the form of vesicles and granules and more or less sharply defined light or dark globules. It is only in rare instances that the gelatinous swelling and final disappearance of the axis-cylinder can be distinctly traced.

When nerve-preparations which have previously been boiled with *alcohol* or *ether* are suffered to remain for a considerable time in a dilute *solution of soda*, the nerve-tubes appear to be considerably contracted, and to become almost perfectly pale; there is very little indication of any granulation in them, and the appearance presented to us is that of contracted nerve-sheaths from which the contents were entirely removed.

The nerve-cells swell in a dilute solution of soda and become paler; in the meanwhile the cell-membrane is frequently rendered more distinct (Kölliker), but after a time the nucleus wholly disappears. When the grey substance of the brain, or any other nervous substance rich in cells, is exposed to the action of a dilute solution of soda, the cells, that is to say, both the walls and the nuclei, wholly disappear, leaving only a more or less finely granular substance.

When the nerve-fibres have lain for a prolonged time in a *concentrated solution of potash*, the whole mass becomes converted, on being well shaken, into a white emulsive fluid; under the microscope, in addition to simple and double outlined, light or dark vesicles, there appear the most complicated forms of this fat-like matter. Although baton-like bodies having double contours, or long filaments varicosely swollen at individual points, become visible, these cannot be regarded by any one who observes them attentively, as the remains of nerve-fibres, for both the sheaths and the axis-cylinders are completely dissolved on prolonged digestion. But when a concentrated solution of potash is added to a fresh preparation of animal or vegetative nerve-fibres, the contents of the individual tubes become granular, the double contours of the animal fibres disappear, and no trace of the axis-cylinder remains. If the preparation is suffered to remain in the air for a prolonged time (until it absorbs water), or if water be added, the outlines disappear gradually, but completely, leaving only serially arranged granules which indicate the former position of the fibres.

When fresh preparations are treated with a concentrated solution of potash, the nerve-cells become slightly contracted, their contents exhibit a more granular appearance, and neither

nucleus nor nucleolus is visible; on the addition of water they are observed to swell up, and the contours gradually to disappear in the fluid; the nuclei do not appear, and at length nothing remains visible but a little granular matter.

When preparations of nerves which have been immersed in *concentrated nitric acid* for any length of time are brought in contact with a dilute *solution of potash*, the granular contents exude in the form of pale drops or globules from the yellow-coloured portions of fibre, leaving only the empty sheaths, which appear to be of an extremely pale yellow colour. This method, which was first suggested by Kölliker, is, perhaps, the best adapted for bringing to view the sheaths of the individual nerve-fibres.

When nerve-fibres, which have been immersed for a considerable time in *concentrated acetic acid*, are treated with boiling ether or alcohol, their appearance is found to differ according as these agents have acted more on small bundles or on individual portions of fibres. The longer portions, or the nerve-fibres that have been separated by the method described in the preceding paragraph, appear to be somewhat contracted when compared with the thick coarsely granular fibres which have been treated with acetic acid only; the pale contours, corresponding to the sheath-membrane, become distinctly visible at certain points; invested in this membrane we see short portions of a granular substance, which are separated from one another by light intermediate spaces; there is usually no axis-cylinder to be recognised in these fibres. If the acetic acid has not exerted its action for too long a time, and especially if it has not been warmed, the axis-cylinder may be very distinctly seen in the torn fragments of a nerve-fibre after it has been treated with alcohol or ether, and its projecting end may be traced for a considerable distance within the tube. Very short portions of nerve-tubes seem, however, to be perfectly empty, appearing like tolerably regular, very faintly granular, extremely transparent cylinders, bearing some resemblance to the urinary cylinders in Bright's disease, which are composed of the *membrana propria* of the tubes of Bellini, only they are far narrower and at least equally hyaline.

If we now proceed to consider the conclusions which may be deduced from the above-described micro-chemical reactions, and from others on a larger scale, we find that the following is the *chemical constitution of the separate morphological constituents* of the nerve-fibres and cells.

The sheath of the nerve-fibres consists, according to the above

observations, of a structureless, somewhat elastic membrane, which does not swell in a gelatinous-like manner in acetic acid, is not dissolved either by boiling or by treatment with dilute alkalies, and cannot, therefore, at all events, consist of pure connective tissue. It dissolves completely in concentrated acetic acid, as well as in solutions of potash and soda after prolonged digestion or boiling, and likewise in concentrated sulphuric acid, but does not dissolve in concentrated nitric acid, which appears to impart a yellow colour to the empty sheaths, although it cannot be distinctly determined by the microscope whether this pale yellow colour proceeds from the sheath itself or from the small quantity of albuminous matter remaining in the partially emptied nerve-fibre. We are thus led to the hypothesis advanced by Mulder* and Kölliker,† that the sheath of the nerve-fibre consists of a substance not unlike elastic tissue, from which it, however, differs by its solubility in boiling acetic acid, and by its greater solubility in a solution of potash. It is very analogous to the substance of the sheath of the primitive bundles of muscles, but resembles a true protein-substance much more nearly than does the elastic tissue.

The *axis-cylinder* consists, according to all the above-mentioned reactions, of a protein-substance which presents many resemblances to the substance of the muscular fibrils (syntonin), although it is certainly not identical with it. The substratum of the axis-cylinder shows itself to be a protein-substance by its behaviour towards acetic acid and very dilute hydrochloric acid, towards dilute and concentrated alkaline solutions, towards concentrated nitric acid and potash, as well as towards concentrated sulphuric acid. This substance differs from ordinary blood-fibrin by the difficulty with which it dissolves in acetic acid, and by its perfect insolubility in carbonate of potash, as well as in a solution of nitre after a prolonged digestion at a temperature of 30°; and it is distinguished from muscle-fibrin (syntonin) by its insolubility in dilute hydrochloric acid, and by the difficulty with which it dissolves in acetic acid. It is scarcely possible to confound it with the substratum of any other elementary tissue. The substratum of elastic tissue is perfectly insoluble in dilute alkalies and in acetic acid. Moreover, the substance of the axis-cylinder cannot be composed of gelatigenous connective tissue; for, independently of the above-described behaviour towards acids and alkalies, it undergoes no change whatever when boiled with water. Least of all

* Vers. einer physiol. Chemie, S. 655 [or English Translation, p. 602].

† Mikrosk. Anat. Bd. 2, S. 397.

could we have expected that any one should regard the axis-cylinder as composed of fat, or at all events, of a very fatty substance, as Mulder and Donders have actually done. The constantly recurring cylindrical form which is observed on the application of the very different reagents which have been mentioned, the great coherence, the elasticity and sharp outline of the axis-cylinder, its complete insolubility in boiling alcohol and ether, its continuous visibility on the application of reagents which expel and dissolve the fat from the nerve-tubes, and, lastly, the entire absence of experimental evidence that a fat can under any circumstances be converted into a consistent and resistent filament, incline us to believe that Mulder's assertion must be ascribed either to a simple error of memory or to a *lapsus calami;* for, although we may not be able to prove definitively that the axis-cylinder is wholly free from fat, the above reactions appear to show beyond a doubt that it consists essentially of a protein-like body, and that the fat which is so abundant in the nerves is principally, and in all probability, entirely accumulated in the nerve-pulp. Kölliker has been led to advocate this view from his investigations regarding the axis-cylinder.

The *medulla or nerve-pulp* appears, as we have already seen, to be perfectly homogeneous in recent preparations of the nerves, and moreover so perfectly transparent, that we can scarcely conceive it to be anything more than a viscid emulsive fluid, although the above indicated micro-chemical reactions, and the behaviour of the nerve-pulp in water, and on exposure to cold, show, that in addition to an abundant supply of fat, it also incloses a protein-substance, permeated by aqueous moisture. I can hardly compare this protein-substance to coagulated albumen, as some other observers have done, for albumen in a state of coagulation would easily admit of being distinguished under the microscope from fat, by the molecular form which it presents in this condition. It may very probably be regarded as corresponding with soluble albumen or casein, for when chemists engaged in analyses of the cerebral substance speak of coagulated albumen, they do not refer to the albumen of the true nerve-pulp, but to the fibrin-like matter of the axis-cylinder. The albuminous substance of the nerve-pulp is, however, entirely different from the matter forming the axis-cylinders. This substance is soluble in, or rather, it may be extracted from the nerve-pulp by a dilute solution of soda, and by acetic acid when not too much diluted; so that after repeated treatment with boiling alcohol or ether, the nerves appear to be perfectly empty, with the

exception of the axis-cylinder. When nerve-fibres have been treated with alcohol or ether, after having been exposed to the action of concentrated nitric acid, or conversely when they have first been treated with nitric acid, and subsequently with a fat-solvent, they still exhibit finely granular yellow-coloured contents, which can be nothing else than this protein-substance, which is now in a coagulated state. I have frequently been at great pains to ascertain the presence of a protein-substance coagulable by boiling or by acetic acid in cerebral matter which had been extracted with water; but from various causes, amongst which may be mentioned the emulsive form which the fluid constantly presented, the blood-serum which it always contained, and the power exerted by acetic acid in decomposing the fatty matters, I was prevented from obtaining any undoubted result. Although it is very difficult to obtain direct proof from microscopical observations, or rather to form a judgment from them, the descriptions of the alterations experienced by the nerve-pulp on the addition of different reagents (in becoming coarsely or finely granular or crystalline) seem to indicate that the nerve-pulp contains a soluble protein-substance in the closest admixture with a fat dissolved by easily decomposable soaps, and that the visibility of the pulp is owing less to the coagulation of this albuminous body than to the separation of the fat from the decomposing soaps and the albuminous substance. It might, indeed, be assumed from the alteration which is gradually perceptible in the pulp of fresh nerves, on exposing them to the action of the air, water, or cold, that a substance similar to the fibrin of the blood was in solution in the fresh nerve, and subsequently coagulated like blood-fibrin; but repeated microscopico-mechanical investigations of the nerve-fibre do not especially favour this hypothesis, for the substance which is separated has always more or less the character of fat, but not that of fibres (like coagulating blood-fibrin), or that of the finest molecular granules (like other protein-bodies in coagulating). For even if we assume such a spontaneous coagulation of the albuminous substance of the nerve-pulp, the undoubted separation of the fat would still remain unexplained, and we should be compelled to have recourse to the preceding conjecture, regarding the separation of the fat from the solution of the salts of the fatty acids. It seems to us, however, that Henle's* view, that the nerve-pulp is not an emulsion, but an actual solution or mixture, leaves no doubt in relation to this question.

* Allg. Anat. S. 624.

It may be observed that Bence Jones* has made an elementary analysis of the residuum which is left after boiling the brain in alcohol, ether, and water, and found that its composition was the same as that of albumen. It is scarcely necessary to remark that in the present state of our knowledge, no conclusions can be deduced from such analyses as these.

The *fats* of the nervous substance can more readily be submitted on a large scale to accurate chemical investigation than any other constituents of the nerve-fibres, but this very circumstance has thrown extraordinary difficulties in the way of inquirers, which have been increased from the fact that the chemical investigation was not simultaneously associated with a careful microscopical examination of the matters that were being chemically treated. Whilst so distinguished a chemist as Couerbe† has distinguished a number of indistinctly characterised fats, as a *cephalot*, *cerebrot*, *stearoconnot*, *eleëncephol*, &c., a no less distinguished chemist, Fremy,‡ arrived at very opposite results, which, although they threw considerable light on this question, did not by any means exhaust the subject in a chemical point of view. Gobley,§ as we have already observed, in vol. i, p. 243, separated phosphate of glycerine from the brain-fat. The following facts are almost the only ones possessing any certainty which have been obtained from the investigations hitherto made in relation to these fats (which were nearly all extracted from the brain). According to Fremy, boiling alcohol will extract from triturated cerebral matter olein and oleic and margaric acids, and fats which are combined in part with soda, potash, or lime; on then digesting the residue with hot ether cholesterin and cerebric and oleophosphoric acids are obtained in solution. The separation of these two groups is not, however, so perfect as might have been supposed from the above remarks; for a considerable amount of cerebric acid and cholesterin passes into the alcoholic solution, whilst oleic and margaric acids are found in the ethereal solution.

Fremy obtained the *cerebric acid* tolerably pure, by again stirring the ethereal extract of the brain with cold ether, from which a white mass separated, which soon assumed a waxy character after decantation of the ether on exposure to the air. The fatty acid

* Ann. d. Ch. u. Pharm. Bd. 40, S. 68 ff.

† Ann. de Chim. et de Phys. 2 Sér., T. 56, p. 164-180.

‡ Journ. de Pharm. T. 26, p. 769-794, and Ann. de Chim. et de Phys., 3 Sér., T. 2, p. 463-488.

§ Journ. de Chim. et de Phys. 3 Sér., T. 11, p. 409-417, et T. 12, p. 5-13.

was combined here with soda and lime; this soap was next dissolved in boiling anhydrous alcohol, and decomposed with a few drops of sulphuric acid. After the sulphates (which contained a little coagulated albumen mixed with them) had been removed by filtration, the hot solution was allowed to cool; from this the cerebric acid separated itself, mixed with a little oleophosphoric acid, which latter substance was removed by means of cold ether, and the cerebric acid once more crystallized in hot ether.

This substance, which Gobley thinks he has also found in the fat of the yolk of egg, forms a glistening white powder, which is insoluble in cold alcohol and ether, but dissolves in both upon boiling. The white granules swell in water. This acid combines with most bases and forms salts, which are perfectly insoluble in water. Fremy found in the dried baryta salt 7·8% of baryta; in 100 parts of the acid, according to separate determinations, 66·7% of carbon, 10·6% of hydrogen, 2·3% of nitrogen, and finally 0·9% of phosphorus. The quantity of oxygen must, therefore, have amounted to about 19·5%, whilst the saturating capacity was about 0·884.

Fremy's *oleophosphoric acid* has been examined even less accurately than cerebric acid. He obtained it by treating the ether-extract of the brain, from which the cerebric acid had been deposited, with cold ether. It remained combined with soda after the ether had been removed by distillation, and presented the appearance of a viscid mass. It appears to be separable from the base by washing with a dilute acid. When isolated, it forms a yellowish viscid mass, which is inflammable, and leaves a bulky carbonaceous residue, from which phosphoric acid may be extracted by water; it is insoluble in water and in cold alcohol; but dissolves in hot alcohol as well as in cold and hot ether. If this acid is boiled with alcoholic solutions of mineral acids or alkalies it is decomposed, according to Fremy, into olein, and oleic and phosphoric acids. Although Chevreul conjectured that the brain-fat might be a combination of olein and phosphoric acid, such a decomposition of oleophosphoric acid is somewhat remarkable, considering our present views of the decomposition of the fats; and indeed, Gobley believes that he has found that oleophosphoric acid yields only oleic acid and phosphate of glycerine, and not olein, during the decomposition which it undergoes during the putrefaction of the brain. This question does not, however, admit of a ready solution, since it is very difficult altogether to free the substance which Fremy terms oleophosphoric acid from the olein and

cerebric acid adhering to it. We may, however, readily convince ourselves that Fremy was mistaken in believing free phosphoric acid to be formed, the substance being, as Gobley has found, phosphate of glycerine. I succeeded on one occasion in most unquestionably demonstrating the presence of phosphate of glycerine in the mass obtained from a very diffused yellow softening of the brain, which, as Rokitansky has shown, contains a free acid. Moreover while Fremy found from 1·9 to 2·0% of phosphoric acid in his oleophosphoric acid, Gobley, on decomposing the same acid by acids and alkalies, always obtained margaric acid in addition to oleic acid,—a proof of the obscurity which still envelopes the whole subject. It seems indeed to be proved, from the observations hitherto made in relation to this question, that the elements of these two kinds of cerebral fats are very unstable, that is to say, that they are extremely prone to numerous decompositions, and that they are mere admixtures of substances of which the one may have served the other as a medium of solution or distribution. The presence of nitrogen in the cerebric acid, and Fremy's assertion that albumen passes into the ethereal solution, are questions which, singularly enough, have hitherto failed to excite observers to any more exact investigations, although they are at variance with preexisting observations, and may very probably be of great significance in reference to the function of the nervous system, which is so immutably combined with its chemistry.

The *cholesterin* which occurs in the fat of the brain is partly taken up by the alcoholic extracts, and partly dissolved by ether, together with the cerebric and oleophosphoric acids, which it accompanies in all their solvents.

The analyses of so careful an observer as Fremy preclude the possibility of doubting that pure olein is contained in brain-fat, although we cannot consider it as demonstrated that this olein is derived from the (so-called) oleophosphoric acid.

The quantity of oleic and margaric acids obtained by Fremy on extracting the brain-fat with alcohol containing ammonia, is very small. When, as is often the case, these fatty acids are found in considerable quantity in the brain, their presence may in reality be owing to the facility with which the brain and its fats are decomposed.

We know but little of the chemical composition of the morphological elements of the nerve-cells, for the micro-chemical reactions already given lead us to very few conclusions on this point. From these observations it appears that the investing membrane of these

cells does not easily dissolve in acetic acid and in alkalies, although it certainly cannot be regarded as entirely insoluble in them. It may, indeed, bear some resemblance to syntonin, for the cell-membrane is insoluble in carbonate of potash, and, as we have already stated, the nerves harden in a solution of this salt. It is worthy of notice in reference to this subject, that the grey, highly cellular substance of the central organs becomes more hardened than the white.

The nuclei of the nerve-cells, like those of most other cells, are rendered more distinctly visible by acids, whilst they disappear in alkalies, without, however, enabling us to form any exact idea of their chemical nature.

It appears from the micro-chemical reactions, which have been previously described, that the semi-fluid granular contents of the nerve-cells are much poorer in fat than the pulp of the nerve-tubes; for after the application of acetic or hydrochloric acid, or other reagents, we perceive a far smaller quantity of coarse granular fatty matter in them than in the nerve-pulp. This observation would appear to acquire corroboration from the smaller quantity of fat in the grey than the white substance of the brain, provided, indeed, that any definite conclusions can be drawn from analyses of entire portions of the brain. All analysts have found only very little fat in the grey substance, which is so rich in cells, whilst in the fibrous medullary substance there is at least four times as much fat present. As, moreover, the contents of the nerve-cells are not rendered much paler by the application of alcohol or ether, their granular appearance must be owing less to fat than to other molecular matters. These granules must not, however, be confounded with those very dark granules, which are insoluble in caustic alkalies, and which we chiefly see in the nerve-cells which are either stellate or provided with long processes or prolongations. These consist of a substance which is still chemically unknown to us, but which is not very dissimilar to pigment-granules. It would appear, therefore, highly probable from the above observations, that the principal part of the contents of the nerve-cells consists of a partly dissolved, and partly only swollen protein-substance.

If we now take a glance at the little that is known regarding the composition of the cerebral and nervous masses generally, the following points present themselves to our notice; we must, however, bear in mind that the cerebral mass contains a large number of blood-vessels and, consequently, a quantity of blood, which must not be included in the analysis.

We were not in possession of any very carefully conducted investigations respecting the amount of *water* and *fat* present in different parts of the brain, until the subject was recently undertaken under Schlossberger's superintendence by Hauff and Walther,* and by von Bibra.† These investigations have led to results which are on the whole of a very conclusive and accordant character. It is perfectly established that the white substance of the brain is much poorer in water and richer in fat than the grey matter. With reference to individual portions of the brain, the quantity of water seems to stand in an inverse ratio to that of the fat. In the cortical substance of the hemispheres Hauff and Walther found from 85 to 86% of water, and only from 4·8 to 4·9% of fat; and von Bibra from 84 to 88% of water, and from 5·5 to 6·5% of fat; whilst the former of these observers found 70·2% of water, and from 14·5 to 15·5% of fat in the white substance of the corpus callosum, the latter obtained from 63·5 to 69·2% of water, and from 20 to 21% of fat. On comparing the quantity of fat and water found by these analysts in the different parts of the brain, we find that it may be pre-determined with tolerable accuracy according to the relative amount of the white and grey substances. The same relation was found to exist not only in man, but in all animals in which the brain is sufficiently large to admit of the analysis of the separated grey and white matter for fat or water. Moreover Lassaigne‡ had previously found that the grey substance was richer in water than the white, the former yielding 85·2%, and the latter only 73·0% of water.

Von Bibra found that in man, as in most animals, the greatest quantity of fat was deposited in the medulla oblongata.

Vauquelin, as well as Fremy, found that the whole brain (grey and white substance mixed) yielded with tolerable uniformity 80% of water and 5% of fat, whilst Denis found only about 78 or 76% of water, but as much as 12 or 13% of fat; von Bibra found on an average 75·54% of water and 14·43% of fat. In animals the quantities of water and fat were found to differ considerably.

Bibra found from 1·5 to 1·9% of *phosphorus* in the brain-fat.

Fremy found 7% of *albuminous matter* in the brain; and Lassaigne 7·5 in the grey cerebral substance, and 9·9% in the white substance.

Lassaigne, singularly enough, found only from 2·2 to 2·3% of

* Ann. d. Ch. u. Pharm. Bd. 85, S. 42-55.

† Ibid. p. 201-224.

‡ Compt. rend. T. 9, p. 703, et T. 11, p. 763.

salts in the brain of an insane patient, whilst, according to Vauquelin and Fremy, 6% is the smallest normal quantity.

Schlossberger* has recently made the remarkable observation on the brain of a child which died at birth, that, in the first place, the corpus callosum in new-born infants is as rich in water as the grey substance; further, that the quantity of fat is nearly the same at this age in the grey and white substance; and, finally, that the brain of new-born infants is generally much richer in water and poorer in fat than the brain of adults.

Schlossberger found that the quantity of water in the brain of the child referred to, varied only in different parts from 87·4 to 89·6%, whilst the fat fluctuated between 4·5 and 3·8%.

When we pause to inquire whether any important conclusions can be deduced from the chemical investigations hitherto instituted in reference to the nervous mass, as to any special function of the nervous system, we are obliged to admit the complete insufficiency of our chemical knowledge. But, however forcibly we may be compelled to admit the incapacity of chemical assistance to explain the actions of the nervous system, chemists will not suffer themselves on that account to be deterred from further investigations; for they must be well aware that, without a careful examination of the chemical phenomena presenting themselves in the nervous system, they can never succeed in tracing nervous action to definite physical laws. The very great significance of the axis-cylinder discovered by Remak, and termed by him "the primitive band," the important discoveries of Dubois regarding electric currents in the nerves, and the minute and ingenious physiological experiments on the different functions of the individual systems of nerve-fibres and cells, will not afford us any deeper scientific insight into the general functions of this most delicate of animal matters, or justify us in establishing definite laws, and not merely individual propositions or rules, until we shall succeed in forming for ourselves a mental representation of the reciprocal actions of the chemical substrata when the nerves are in a state of activity. If observers should ever succeed in detecting the presence in the nerves of a peculiar agent, active only in living animals, or if the propagation of nerve-force, and the corresponding phenomena of reflex action, irradiation, &c., should be found to depend upon electrical currents passing through cylinders endowed with more or less thoroughly isolating walls, chemistry must still be called to our aid if we wish to obtain an exact physical explanation of such phenomena.

* Ann. d. Ch. u. Pharm. Bd. 86, S. 119-125.

Chemistry is too intimately associated with all the most important questions concerning the theory of the nerves to be excluded from its just participation in the study of that most noble of all animal matters in which are concentrated the highest vital functions. The share taken by chemistry in the explanation of the functions of the nervous system is now so thoroughly and fully admitted that it is unnecessary to enlarge upon this point. In correspondence with the physical and physiological phenomena of the nerves, we find a substance accumulated in them which exhibits such mobility in reference to its proximate constituents as is not to be met with in any other organ of the animal body; the chemical phenomena very probably, therefore, stand also here in the closest relation to the physical and physiological. Scarcely any one can entertain the idea that the nerves which (as Ludwig* has shown in his admirable Memoir on the influence of the nerves upon the salivary secretion) co-operate directly in the elaboration of certain secretions from the blood, and influence their accelerated or modified separation, can control such functions without undergoing chemical change. The chemical substrata of the nerves are conformable to their functions; for, as in all other organs, the physiological importance of the chemical constitution, and the relations of affinity between the chemical substrata, must accord with one another. (See vol. i, p. 25.)

The *analysis* of the nervous tissue is obviously still very imperfect, as must be seen from the above remarks.

The most suitable object for an investigation of this kind is probably the white matter of the hemispheres of the cerebrum, if we have reference only to the facility with which considerable quantities of it may be obtained. The white matter is far preferable to the grey, as it contains fewer blood-vessels, no nerve-cells, and scarcely anything but nerve-fibres.

In making the determination of the quantity of water, the same precautions are required as in the case of every other organ, and especially of the muscles. We have already shown the importance of such precautions in our observations on the latter organs.

In determining the mineral constituents of the cerebral matter, it must be borne in mind that the ash exhibits an acid reaction from the presence of free phosphoric acid, and that it, on that account, generally encloses a considerable amount of carbon. As is well known, phosphorus is given off in a volatile form when carbon is heated with phosphoric acid or with acid phosphates,

* Mitth. d. Zürch. naturf. Gesellschaft. No. 50, 1851.

and any metallic chlorides or phosphates which may be present, are simultaneously decomposed; hence it is absolutely necessary to triturate the dried cerebral mass before its incineration with a little carbonate of baryta—a precaution which will prevent any kind of loss.

The most rational method of separating the organic, and especially the morphological elements, and the one which accords most closely with the micro-chemical reactions, is to treat the triturated cerebral mass with a dilute solution of carbonate of potash, as this solution does not attack the axis-cylinder or the nerve-sheath, and alters the nerve-pulp less than any other reagents, inasmuch as it simply dissolves the albuminous substance and the greater part of the medullary fat; the filtered fluid certainly passes in a turbid state through the filter, just as when pure water is used in place of the above reagent, but here a much smaller quantity of fat is held in suspension, and a much larger amount actually dissolved. Mere traces only of histological elements, and often not even these, penetrate through the filter, and after repeated rinsings with the solution of carbonate of potash there remains on the filter only a very little fat (principally a little cerebric acid) with the other organic matters. The albuminous substance of the nerve-pulp may easily be detected in the solution by means of the ordinary reagents after the fluid has been saturated with acetic acid, the precipitate separated by filtration, and the suspended fat removed by ether.

The residue of the cerebral mass, which is insoluble in carbonate of potash, and, besides a part of the cerebric acid, contains only the axis-cylinders and the nerve-sheaths, must be heated in a dilute solution of potash or soda for the purpose of dissolving the acid; from this solution the albuminous substance of the axis-cylinders, together with a little cerebric acid, is precipitated by acids, with the development of a little sulphuretted hydrogen.

The residue of the cerebral matter, which is insoluble in dilute solutions of the caustic alkalies and their carbonates, contains scarcely anything but the nerve-sheaths and a little cerebrate of lime, the latter of which may be removed by boiling this residue first with dilute acetic acid, and subsequently with ether. We cannot, however, unfortunately consider this residue as a chemically pure substratum of the nerve-sheaths, as the walls of the capillaries are intermixed with it.

The methods of investigation which we have described do not, however, as we stated, suffice to separate the cerebral fats in any rational manner from one another; nor can we hope to see good

methods employed for quantitative separation until the chemical constituents of the cerebral and nervous matter shall have been determined with much greater exactness.

[I have just received a copy of a Memoir by von Bibra, entitled "Comparative Investigations of the Brain of Man and the Mammalia;" * his principal conclusions will be given in a note to Appendix. Much interesting matter upon the subjects discussed in this section will also be found in Schlossberger's Memoir on the Nervous System in his "First Attempt at a General and Comparative Animal Chemistry," † which is now in the course of publication.—G. E. D.]

Exudations and Pathological Formations.

We have often had occasion to comment upon the inefficiency and imperfection of our chemical knowledge, when compared with the great expectations which have been entertained in respect to its applications to physiology and pathology; yet there is scarcely any subject which more thoroughly calls for a confession of our weakness and incapacity than the one we are now about to consider. The exudations constitute the most important object of zoo-chemical investigation in reference to pathology, and the whole scope of pathological anatomy may be said to consist in the study of these structures and their different metamorphoses. But whilst pathological morphology may be said to have already reached a very high degree of development, the chemistry of morbid structures is still very obscure. The history of the development of pathological forms has contributed very little to clear up these difficulties, notwithstanding the great advance which this branch of science has made in recent times; and it is an undeniable fact that in the case of many pathological forms we are wholly ignorant whether we have before us the beginning or the end of the process, the first formation, or the last stage of disintegration. The science of pathological histology, which alone can guide the chemist, is so full of uncertainties, subjective conceptions, and varying con-

* Vergleichende Untersuchungen über das Gehirn des Menschen und der Wirbelthiere. Von Dr. Freiherrn Ernst von Bibra. Mannheim, 1854.

† Erster Versuch einer allgemeinen und vergleichenden Thier chemie. Von Julius Eugen Schlossberger. Erste Lieferung. Stuttgart, 1854.

jectures, notwithstanding some signal advances, that it scarcely ever presents any starting point for chemical investigation. Few attempts have been made to institute a micro-chemical analysis even of the simplest pathological forms, and how can the chemist, if he have no certain point to start from, arrive at correct conclusions amidst opposing opinions, and the most variable forms and the apparently similar products of the most widely differing processes? Let the chemist once obtain a fixed basis on which to found his inquiries, and he will not fail to resolve purely physical processes into tangible phenomena.

It must be admitted, however, that the causes which prevent the chemist from responding to the demands of the theoretical physician do not depend solely upon deficiencies of physical proofs and pathological observations, but upon an obscurity in the corresponding departments of chemistry. We have endeavoured (see vol. i, p. 19) to explain the causes which prevent chemistry from participating in the investigation of pathological matters, and we would indicate some points which may serve to justify the mode of treatment we have adopted in this chapter, and to explain the inefficiency of chemistry to solve pathological inquiries.

We referred, in the introduction to histo-chemistry, to our very deficient knowledge of the protein-bodies as the principal cause of our inability to comprehend the elaboration of the tissues; yet the metamorphoses of the protein-bodies of the blood play the principal part in the pathological exudations, cells, and tissues. It therefore appertains to the chemist to follow the individual metamorphic stages in each of these bodies, as the histologist endeavours to trace the gradual formation of morphological elements in their metamorphosis into cells and tissues. But whilst the parent substances, and their relations to one another, are so imperfectly known that we cannot, with any certainty, attempt to establish for them a chemically rational formula, we have but little prospect of being able to elucidate their proximate derivatives and the relations of affinity they bear to one another. The prospect would be less discouraging if we were as well acquainted with the first stages of metamorphosis as with the protein-bodies themselves. It should be remembered how difficult it is to distinguish albumen and casein when they are associated in the yolk of egg and elsewhere; that casein itself appears to be a mixture of several substances; and lastly, that it is a matter of extreme difficulty, indeed almost an impracticable operation, to extract chemically demonstrable substances from pathological products—whether recent or older

exudations. Even in those cases in which the chemist succeeds in extracting one or other of these substances, he seldom obtains satisfactory evidence of their chemical purity, without which they are wholly inapplicable for a true chemical investigation. A chemist cannot be satisfied that he knows a substance until he has submitted it to an elementary analysis, and can attain, at all events, an approximate determination of its atomic weight; in fact, a body which has been submitted by the chemist to a few reactions only, however striking they may be, but for which he is unable to establish a formula based upon elementary analysis, may be almost considered as unknown to him. In this sense (and in exact investigations we can only take this view) all substances which manifest themselves as transition-stages from the protein-bodies of a plastic exudation are wholly unknown to us, and must remain equally unexplained until we are able to elucidate the mystery of protein.

Although there may be an established conviction that the chemist is still unable to trace the metamorphoses of plastic matter in the exudations, and to note the processes by means of which one or other form is produced, we may be disposed to inquire what qualitative alterations, what heterogeneous constituents, and what special substances are to be perceived in the inflammatory, or the so-called specific exudations.

Like others, we have undertaken numerous investigations of this subject in obedience to the requirements of physicians, and we have succeeded in proving the presence of true biliary substances both in plastic and non-plastic exudations under many different relations, which scarcely admit at all times of being fully demonstrated, and have exhibited taurocholate of soda as well as beautiful crystals of glycocholate of soda. Urea, sugar, certain extractive matters, &c., may be shown to exist in nearly all exudations. However interesting such observations may be in many respects, the presence of these substances can scarcely, as far as we are at present able to judge, have any important influence on the metamorphosis of the fluid exudation, or any special signification in respect to the formation of this or that form of tissue. What additional point have we ascertained if even we succeed in showing that cystine forms the principal constituent in tuberculous masses, succinic acid possibly in cancerous growths, or some other unusual substance in other diseased matters, if no connection can be traced between the presence of such a substance and the other circumstances of the case? The qualitative examination of patho-

logical products is, moreover, essentially obstructed by numerous relations. Every pathologist knows how rare it is to meet with very recent exudations in the dead body; how difficult it generally is to determine the age of an exudation, even with any degree of accuracy; how insufficient, even under the most favourable circumstances, is the quantity of the material in which we have to seek for special constituents; and how rapidly decomposition sets in after death, even while the body is yet warm.

We would here touch upon only one of these impediments. We have already often had occasion to notice in this work the admirable contributions made by Liebig to our knowledge of the metamorphosis of animal matter by his investigation of the muscular fluid; these experiments were, however, conducted under very favourable circumstances; for independently of his genius and dexterity, we need only refer to the mass of the material which he employed, and to the fact that perfectly fresh materials and analogous objects could be easily procured for comparison. It was reserved for Liebig and Schlossberger to re-discover creatine, to which Chevreul had long before drawn attention, whilst to them also belongs the merit of making us more intimately acquainted with its nature. Notwithstanding the favourable circumstances already indicated, Liebig himself was only able to indicate a few substances, as inosic acid, &c. Moreover, Scherer's inosite can only be exhibited when we have large quantities of material at command; and it seems, as it were, to evade the experimenter, by becoming converted into butyric acid, if the fresh material and the separate extracts are not carefully guarded from the risk of decomposition. In a word, whilst even the qualitative investigation of objects derived from healthy animals has to contend with such difficulties that very few animal juices admit of being very accurately examined, the qualitative analysis of pathological products is opposed by insurmountable obstacles.* We must, therefore, wait till the physiological juices and their metamorphoses in the animal body have been more attentively studied, before we venture to submit the solid or fluid pathological products, the more or less remote allies of the blood and of its protein-bodies, to a truly scientific qualitative investigation.

If we have, therefore, very slight prospect of being able to trace pathological processes by a qualitative examination of exudations, or of attaining any scientific aim by such a mode of procedure, we are led to inquire, with some hesitation, whether the quantitative analysis of these products would be attended by any better

result. On closely considering the question, we certainly find that the quantitative investigation of the exudations justifies us in entertaining far higher hopes, and that it opens to us a rich and varied field of inquiry, while at the same time it affords but little encouragement to the present tendency of physicians towards humoral pathology. We must here rather abide by physical laws, which will afford us the best and securest support in our endeavours to give a more general character to the results of such inquiries. But here we have first to determine the points of view from which such quantitative investigations of pathological products should be considered, as long as our knowledge of qualitative analysis is so deficient.

We endeavoured, under the head of Animal Juices (vol. ii, p. 308, &c.), to distinguish excessive transudations from exudations, although we did not believe that any very strictly defined line of demarcation could be drawn in individual cases between these two kinds of fluids, which are both exuded from the blood. If we exclude from our consideration the transitional forms, those differences to which we have referred (see above), and which have been more than sufficiently described by pathologists and histologists in the distinctions between plastic and non-plastic exudations, are rendered sufficiently prominent. We have endeavoured to show, from our own experiments and those of others, that the formation and constitution of transudations depended upon certain physical relations. We think we shall scarcely be in error if we assume that definite numerically reducible relations will be discovered for the exudations, by which their composition and subsequent metamorphosis may be established. In short, no one who is not dazzled by the fantastic forces, which have been supposed, during the last few years, to play so prominent a part in the animal body, can doubt that these exudations are subjected to definite, physically determinable laws. Although the nervous influence may act in a tolerably direct manner upon the chemical relations of the exudation, the quantitative relations must solely depend here, as in all similar processes of the animal body, upon alterations in the mechanical relations. When, therefore, we have investigated the quantitative relations of the products, we shall undoubtedly find enough certain results to give us some insight into the mechanical conditions. It will of course be understood that we do not, in the least, underrate the great theoretical difficulties which present themselves in this inquiry; the task we propose to ourselves is the simple one of solving the question of the

connexion between the quantitative relations of the exudations and the mechanical conditions necessary for their formation.

Perfect as in many respects the phenomenology of the exudative process may be already considered, obvious as are the mechanical conditions which give rise to exudation as well as to transudation, and great as have been the advances made in our endeavours to trace the laws by which the most minute fluid particles distribute themselves through membranes or through other fluids, and strive reciprocally to establish themselves in a certain equilibrium, we can yet never expect to obtain an inductive proof for our mechanical hypotheses until we can succeed in making the quantitative composition of the products of these processes harmonize with the laws or provisional hypotheses which we have elsewhere endeavoured to establish. The labours of some of the most distinguished physiologists have afforded us considerable insight into the knowledge of the phenomena which exhibit themselves both around and within the capillaries during the existence of the inflammatory process which precedes the exudation. The disturbances of the circulation, whose hydraulic laws have been traced even in the smallest of these tubes, have not yet been followed to their individual controlling causes, and much difference of opinion still prevails in relation to this subject; but there is no lack of elements having a physical basis which may serve to explain these phenomena. In close connection with changes in the modulus of elasticity of the capillary walls there are a number of phenomena which we may very frequently show, with almost mathematical exactness, to be mechanically necessary consequences of these changes. We would here merely indicate, amongst the most recent investigations relating to physiological mechanics, the able inquiries of Jolly* and Ludwig† on endosmosis and endosmotic equivalents, C. Schmidt's‡ experiments on the relation between the coefficients of density and equivalents of diffusion of saline solutions, and Graham's § remarkable discoveries in relation to the diffusion of dissolved substances. If to these we add the recent classical investigations of Volkmann ||, and E. H. Weber¶ on hæmatodynamics and the well-known investigations of Du Bois

* Zeitsch. f. rat. Med. Bd. 7, S. 83-148.

† Ibid. Vol. 8, pp. 1-52.

‡ Charakteristik der Cholera. S. 22-28.

§ Ann. d. Ch. u. Pharm. Bd. 77, S. 56-89, u. 129-160, [or Phil. Trans. for 1850, p. 1].

|| Die Hæmodynamik nach Versuchen. Leipzig, 1850.

¶ Ber. der k. sächs. Ges. d. Wiss. 1850, S. 164-204.

Reymond,* we shall have sufficient materials at our command for tracing the abnormal as well as the normal circulation of matter in the animal body to purely mechanical conditions. But all these new discoveries, and the observations of earlier inquirers, only yield us a number of hypotheses regarding the mechanical metamorphosis of matter; but the inductive proof of their accuracy can only be obtained by means of a series of systematically conducted quantitative analyses of the animal fluids.

If we would investigate the alterations which occur in exudations, and the laws by which these changes are regulated and controlled, it is obvious that we must direct our attention not only to the exudations themselves, but also to the mother-fluid from which the exudations are derived, namely, the blood. It is obvious that it is only by the juxtaposition of the analysis of the exudation and of the corresponding blood, that any value can be attached to the results of the former. The analyses of such exudations should, however, be capable of comparison with one another, and not conducted at hazard merely when the physician may happen to meet with some interesting case.

It may appear superfluous to those who know that the result of an experiment nearly always depends upon the method employed in the inquiry, if we venture to suggest that an accurate investigation of the exudations demands a strictly systematic mode of treatment, or, in other words, an elaboration of the subject from definite points of view, requiring the most careful consideration of all the conditions involved, with a constant regard to the length of time the exudations have existed, the nature of the products exuded, the morphological metamorphoses exhibited by the latter, and many other similar relations. If any apology be necessary for these remarks, we would only observe that, to our knowledge, no one has ever attempted to conduct the examination of the exudations in the above-described rational manner.

We may be permitted to ask, with some show of reason, whether the quantitative analyses of the animal juices are at present conducted in so perfect a manner as to satisfy the requirements for which they are instituted.

We have already considered at length, in different parts of this work, the results which may be yielded by quantitative zoo-chemical analyses, while we have shown, in no very favourable colours, the fruits which they have actually afforded us; but although they fall far short of our expectations, they are yet fully sufficient to

* Unters. über thierische Elektricität. Berl. 1848-49.

answer some of the most pressing questions; for the most important substances are precisely those which are conspicuous by the quantity in which they present themselves for observation; thus, for instance, the insoluble and coagulable protein-bodies, the fats, the collective mass of organic substances soluble only in water, or soluble both in water and alcohol, certain organic acids, and the mineral constituents generally, are perfectly accessible to exact quantitative determinations, as has been recently shown by von Gorup-Besanez* in his admirable treatise on zoo-chemical analysis. As the mineral constituents certainly seem to present a field of the greatest promise, they should be first and especially investigated. We know from the study of the transudations and the animal fluids generally, that the distribution of the potash and soda salts on the one hand, and that of the phosphates and metallic chlorides on the other, is very far from uniform in the different animal juices, and we are almost constrained to follow out this subject more at length, since Graham's investigations have directed our attention to the great inequality in the diffusibility of these substances, and Schmidt's determinations have indicated the difference of the coefficients of condensation of saline solutions when compared with this inequality. The determinations of the organic matters, as for instance, the soluble protein-bodies (accompanied by acids or alkalies) and the fats, will yield far more important results than one might at first sight be inclined to anticipate. If, therefore, the chemist freely confesses his incapacity for the prosecution of qualitative analyses of pathological products, and would gladly abstain from attempting them, he has, on the other hand, before him a vast field of noble, although less arduous labours, with the certain prospect of being able to enrich physiology and pathology with the most brilliant results.

If the difficulties we have indicated in the qualitative investigation of the exudations deter the chemist from prosecuting such inquiries, he will not fail to perceive the great number of difficulties which obstruct his progress when he enters upon the determination of the quantitative relations of the blood, and its more or less abnormal derivatives. Independently of those difficulties, which from the nature of the case appertain to the scientific means employed, external relations necessarily present numerous obstacles in the way of such an inquiry. Although large hospitals and extensive pathological materials are by no means always requisite for

* Anleitung zur zoochemischen Analyse. Erlangen, 1850, [or Second Edition, enlarged, 1854].

the prosecution of investigations which may be productive of great results to pathology, if an experimentalist were desirous of analysing exudations in accordance with the points of view we have been considering, he would of course feel the want of the necessary material in the neighbourhood of merely a small hospital; for in every case the investigation should begin with the most recent exudations, and it is precisely these which are the most rarely met with. In addition to the age of the exudation, other points have also to be observed; for the exudative matters yielded by similar cavities and tissues, ought to be compared together, which it would not be easy to do in small establishments, whilst the accompanying morbid processes, to which the physician attaches the greatest weight, ought to be noted, together with the stages of the exudation and the cavities or organs in which the effusion occurs; but for these purposes we require a larger amount of materials than can often be obtained. If, moreover, the chemist should have the misfortune to be associated with physicians who have a prejudice against venesection, however much theory and practice may favour its adoption, he will be compelled to relinquish the examination of the exudations, for unless he has obtained a previous blood-analysis, such an investigation will be of no value. One of the greatest difficulties which present themselves in the way of obtaining materials necessary for these observations is the circumstance that either from regulations connected with medical jurisprudence, feelings of humanity, or other considerations, examinations are not undertaken until twenty-four hours, or even a longer interval after death, a period within which various processes of decomposition may have set in, and the alterations produced by death may have attained a very high degree of intensity by diffusion and endosmosis. Many of these impediments might be obviated by conducting such experiments as we have described in the neighbourhood of large veterinary institutions, and indeed the advantages of employing diseased animals for such investigations are so obvious that it seems wholly superfluous to refer more fully to them in the present place. Unfortunately, however, very few pathologico-chemical investigations have been prosecuted in institutions of this kind; we must hope, however, that they may speedily be made to contribute towards the establishment of a rational pathological chemistry, since institutions of this class afford much more abundant available materials than hospitals even, for the analyses of the blood. Some of the principal difficulties which we have enumerated present themselves even when we have an abun-

dance of diseased animals at our disposal, for all exudations taken indiscriminately are not equally suitable for a rational investigation, since anatomico-physical relations often render it perfectly impossible to exhibit the object in a pure state.

When we consider the difficulties which present themselves at the very outset of all attempts at quantitative examinations of the exudations, we can hardly wonder that many chemists should shrink from the prosecution of such unsatisfactory labours, more especially when we bear in mind that pathology offers for our consideration numerous questions, the solution of which promises more abundant results, and should, as is obvious to reason, precede the analysis of the exudations. It is to be hoped, that physicians will acquire sufficient insight into chemical and physiological science to avoid propounding questions which without admitting of any exact solution, only bring to light the ignorance of those with whom they have originated, whilst it is equally to be desired that chemists, whether they be expert or not, will avoid placing themselves as mere tools in the hands of their pathological brethren, and increasing the mass of crippled facts and perverted deductions with which pathological chemistry is already overburdened.

From this somewhat prolix introduction to the mode of investigating exudations from a physiologico-chemical point of view, it will be clearly seen, that our positive knowledge in this department of science is extremely small, whilst the majority of the few materials collected in reference to these subjects of inquiry (as, for instance, some wholly irrelevant analyses of cancerous tumours, pleuritic exudations, tuberculous masses, peritoneal exudations of doubtful character, &c., &c.) must be rejected as entirely worthless. We can, therefore, only give a very fragmentary sketch of the subject, and we think we shall scarcely be in error if we wholly omit, or at most only glance at, the ordinary descriptions of the histological conformation, or the microscopical characters of the pathological objects referred to, under the heads of the respective physiological tissues; without such a precaution we fear we might incur the risk of giving a mere outline of pathological histology which would wholly mask the pathologico-chemical nature of the objects under examination. As there is often but little to be said in reference to the chemistry, we shall frequently be compelled to give a histological introduction without being able to describe the chemical composition. If any chemist should be disposed to direct his attention and energies to this intricate department of

science, he will nowhere find a better guide than in Henle's recent and masterly exposition of this subject,* where the accumulated stores of histological materials have been carefully sifted, the objects clearly delineated, and the various points of the inquiry ably treated.

Since the exudations manifest every variety of difference, partly in reference to their morphological characters, partly in the metamorphoses which they undergo, and partly from their different modes of origin, and since we are still far from comprehending their differences from a chemical point of view, the only principle to be adopted in making a division of the whole subject is to choose a plan of arrangement based upon direct observation of the characteristic differences which exist in the physical properties of the objects. Great as has been the labour expended in the attempts to describe and classify the exudations in accordance with their external characteristics, we think the chemist can find no safer guide than that most accurate pathologist Rokitansky.† For although the description which Rokitansky gives of the differences of the exudations may be interwoven with designations and the indications of a theory of crases which the chemist does not recognise, we nevertheless meet with the most minute observations which are perfectly true to nature, and which alone ought to form the basis of a more extended physico-chemical investigation. We therefore purpose following Rokitansky's mode of arrangement in giving the few known chemical relations; and shall consider the exudations 1, as fibrinous, which are again subdivided into simple plastic and croupous; 2, as albuminous; and 3, as purulent, under which head are included ichorous and hæmorrhagic exudations.

The attacks which have been made by many of our chemical physicians against Rokitansky's mode of considering and classifying the exudations, apply less to his own views than to those of some of his pupils and followers, who have distorted his facts by the most wild and paradoxical hypotheses. In reference, however, to any objections which may be advanced against the mode of expression adopted by the founder of pathological anatomy, it should be observed that the expressions *albuminous* or *serous* exudations are intended simply to designate a physically and definitively characterised form of exudation; but that Rokitansky had

* Handb. d. rationellen Pathologie. Braunschw. Bd. 2, S. 667-832.

† Handb. d. allgem. pathol. Anatomie. Bd. 1, S. 194-224, and in other places.

no idea of employing them to designate the internal composition of these objects. A mineralogist might in a similar manner accuse Rokitansky of want of scientific accuracy in applying the term hard to certain new formations, although they are actually softer than the least hard substance in the mineralogical scale of hardness. We do not, however, wish to enter the field against those who are entitled from personal acquaintance with pathology and pathological anatomy, and from independent research, to pass judgment on Rokitansky's systematic arrangement and the craseology on which it is based; but we certainly are of opinion that a system cannot be established without the aid of hypothetical modes of conception, and on this account we have adhered to the mode of representation adopted by this experienced and careful observer.

The *fibrinous plastic exudation* is the only one which can be easily obtained in a perfectly fresh and tolerably pure state. Fresh wounds afford the best means of obtaining it after the hæmorrhage has been arrested, that is to say, when thrombi have formed in the smaller vessels. It can be obtained, however, in larger quantities from animals after portions of muscle have been cut away under the skin, and, consequently, from wounds with a loss of substance. A perfectly fresh exudation of this kind exhibits all the physical and chemical characters of the intercellular substance of the blood. The fluid is faintly opalescent, of a sickly taste, alkaline, and in a short time there is a separation of a colourless, trembling, gelatinous mass. Provided the exudation has been obtained perfectly free from blood, which is not always easily accomplished, no morphological elements can be discovered in it besides the fibrin, which coagulates as in fresh blood. If the fluid obtained from the subcutaneous wounds (with loss of substance) is not perfectly fresh, we perceive in about half an hour or an hour granules and nuclei, which constitute the beginning of the suppurative process. These secretions from wounds are therefore obtained in the greatest purity from animals which are little or not at all prone to suppuration, as, for instance, from birds. Frogs cannot be used for such experiments in consequence of the large quantity of lymph which is poured into the secretion in these animals from the subcutaneous lymphatics.

The constituents of these perfectly fresh exudations do not differ in *quality* from those of the liquor sanguinis. The same substances which impede the rapid coagulation of the fibrin of the blood either retard or prevent the coagulation of the fibrin of the exudations (see vol. i, p. 348). The spontaneously coagulated

fibrin becomes perfectly dissolved after digestion for some time at a temperature of 30° in a solution of nitre, being converted into a coagulable fluid. In water containing hydrochloric acid, the exudation swells up in a gelatinous form, but does not dissolve, in which respect, as in all other reactions, it perfectly coincides with the blood-fibrin. Precisely the similar remark applies to the albumen; and the mineral constituents, in as far as we can determine them from the small quantities of these exudations generally at our command, differ in no essential respect from those occurring in the liquor sanguinis.

No detailed *quantitative analysis* can be made with very recent exudations owing to the small quantities in which they are obtained. I have, however, constantly found more water in them than in the liquor sanguinis, which is the more striking, seeing that in collecting these fluids the evaporation of the water cannot be so readily prevented as when the blood is drawn from the opened vein. In five experiments on rabbits and in three on geese, I found from 1·94 to 4·28% more water in the secretion from the wound than in the plasma of the mixed blood, that is to say, of the mixture of arterial and venous blood, which was obtained from the carotid and jugular vein. I could not determine with any degree of certainty whether the amount of *fibrin* in the exudation was greater or less than that in the liquor sanguinis; but the quantity of *albumen* was decidedly somewhat smaller than in the blood-serum, the difference being greater than could be accounted for by the relative increase of water in the exudation. In geese there was always rather more *fat* in the exudation than in the corresponding liquor sanguinis; but here it was difficult to determine whether the fat from the subcutaneous cellular tissue was not in part mixed with the secretion from the wound. No difference could be detected in the quantity of *salts* contained in both fluids. Strict determinations in the case of the *phosphates* and *metallic chlorides* on the one hand, or of the *soda* and *potash salts* on the other, were impracticable; but I endeavoured in six cases to determine the average proportions of these substances in the secretion from the wound and in the corresponding blood-serum, and I think that I am scarcely in error in stating that the secretion from the wound contains relatively more of the phosphates and potash salts, and that the serum contains an excess of soda salts and chlorides.

The very recent exudations obtained in rare cases from the serous sacs of human subjects present very different relations, not

being homogeneous, but already separated into a coagulum and a fluid.

The *coagulum* varies very much in form and colour according to the relations under which it is separated, and the quantity of blood which it contains. The microscopical characters are generally, or indeed principally, the same as those of spontaneously coagulated fibrin, but in addition to the somewhat swollen, almost spherical blood-corpuscles, there occur certain other morphological structures, as, for instance, granules, clots, nuclear structures, and occasionally also cytoïd corpuscles. The coagulum swells in water containing hydrochloric acid as well as in dilute acetic acid, but it does not form a gelatinous mass of such perfect translucence as the fibrin of the blood, or as that of the secretion from a wound. If the coagulum, after having been comminuted and carefully washed, be digested with a dilute solution of nitre, we certainly obtain a fluid coagulable by heat, although some portion of it always remains undissolved in the menstruum in the form of dirty greyish flakes.

The fluid portion of the more recent plastic exudations is generally clear and transparent; it only becomes opalescent and turbid after the exudation has remained for some time in the cavity. The reaction is commonly less strongly alkaline than that of the blood-serum; it, however, coagulates on boiling, not into minute flakes, but generally into curd-like clots, or into a milky or whitish gelatinous mass. The fluid occurring above the curd-like flakes is strongly opalescent, and even whitish; it passes with difficulty through the filter, which it very quickly obstructs; it forms, on evaporation, the so-called casein-membranes. Acetic acid does not enable us to detect any casein, and the originally limpid fluid is rendered only slightly turbid on careful neutralisation with acetic acid; but this turbidity disappears instantly on the addition of a little more dilute acetic acid. The application of rennet only affords negative evidence regarding the presence of casein. The salts and extractive matters differ in no respect from those occurring in the blood-serum.

The *quantitative composition* of these exudations, when compared with that of the corresponding blood, is far more unstable than that of fresh wound-secretions obtained from animals. The quantity of the *fibrin* does not even admit of being determined approximately, for independently of the fact that such fibrin (that is to say, the coagulated portion of the exudation) contains insoluble morphological constituents, which cannot be washed

out by water, and which cannot possibly be regarded as fibrin, the exudation cannot generally be obtained as an entire mass, that is to say, all the solidified as well as the still fluid parts cannot be removed from the cavity into which they have been effused. In the meanwhile it would appear, from approximate determinations, that the relation between the solidified and fluid matters varies very considerably, a circumstance which confirms the well-known experience derived from personal observation that a large proportion of the exudative fluid is soon resorbed. According to our experience, there is no definite relation between the part of the exudation which remains fluid and the serum of the corresponding blood; but in most cases, here as well as in the secretions from wounds, the solid residue of the exudation-fluid is inconsiderable, and consequently the amount of *water* is greater. I found this difference between the fluids the greatest, namely, about 3·47% in a very fresh peritoneal exudation. In some cases, however, the quantity of the solid constituents in the exudations exceeded that in the corresponding blood-serum. There was usually less of the *coagulable protein-substances* in the exudative fluid than in the corresponding blood-serum; an apparent excess of these substances occurred only in one-seventh of the cases observed, but then the fluid had become turbid, and had not been thoroughly cleared by previous filtration. These fluids differed less in respect to the *extractive matters* which they contained; indeed, if the latter were considered in reference to the quantity of water in both fluids, the difference was in most cases so inconsiderable that it could scarcely be said to exceed the amount of such errors as are unavoidable in observations of this nature. But on comparing them in their relation to the solid residue, we commonly find that there is a small excess for the extractive matters of the exudations. The sum of the *salts* is generally somewhat higher in the exudations than in the blood-serum of the same individuals. On comparing together the different salts we find, without exception, relatively and absolutely more of the *phosphates* and *potash-salts* in all these exudations than in the blood-serum.

However much one might be disposed, from these results of my analyses, to find a confirmation of the view that has already been advanced elsewhere, that the phosphates, and with them probably also the potash-salts, contribute very essentially towards the plasticity of the exudations, we cannot regard the point as definitively settled, for it is not easy to determine to what extent the quantity of blood-cells in the exudations contributes to this

result. I have met with no single plastic exudation (I refer to those only which I examined under the microscope) which did not exhibit a larger or smaller amount of strongly tinged, unaltered, or pale, rounded blood-corpuscles. As, moreover, the blood-corpuscles never continue to be developed in a plastic exudation, but, on the contrary, seem rather to disappear, the proximate cause of this excess of phosphates and potash-salts might therefore be sought in the disintegration of the blood-cells contained in the exudation; for we know that it is the blood-cells principally which contain the phosphates and potash-salts (see vol. ii, p. 189). In point of fact, a comparison between my different analyses will show that the exudations which contained a large amount of blood-cells exhibited a greater proportion of these salts than those which were poorer in blood-cells. The observations made by different physiologists on the relations between the capillaries and the blood contained in them during the inflammatory process lead us to expect that blood-corpuscles will always be present in exudations. Although the constant occurrence of blood-corpuscles in the true plastic exudations, as noticed in the bodies of men or animals after death, would seem to favour the conclusion that the plasticity of the exudations depends principally on the quantity of blood-corpuscles which they contain, such a view is controverted by the fact that exudations which are very rich in blood are not in general the most plastic; and that, as we have already seen, when considering the secretions from wounds, an exudation may be plastic without containing blood-cells. If, therefore, we cannot assert that the blood-cells, as such, together with the fibrin, are the direct cause of the plasticity of the exudations, they at all events appear, from the above-mentioned positive observations, to stand in some indirect relation to the plasticity. For where are we to seek for the source of the excess of potash-salts and phosphates which is constantly present in the plastic exudations, if not in the blood-corpuscles? Even in those wound-secretions, in which we can find no blood-cells, we must refer these salts to blood-corpuscles which have passed into a condition of stasis and solution in the capillaries surrounding the focus of exudation. The phosphates and potash-salts originating from the remains of the blood-cells must therefore penetrate through the walls of the inflamed capillaries, and thus contribute towards the plasticity of an exudation containing no blood-corpuscles. This at the same time explains the cause why the transudations, even when they contain fibrin and some blood-corpuscles, are not plastic, for the separation of

the transudations is not preceded or accompanied by a true inflammatory process with complete stasis and with the entire destruction of the blood-cells in the capillaries, as is always the case in the exudations.

We do not, however, think that it has been satisfactorily proved that the plasticity of the exudation is necessarily dependent upon the presence of these salts, but it is a characteristic of the human mind to catch at the slightest facts for support in the arduous paths of enquiry. Some aid might perhaps be afforded towards the establishment of inductive proof by the results of a series of experiments which I instituted on the blood of horses, comparing the blood of different vessels with the arterial blood. The results of the comparative analyses of eighteen samples of blood from different veins showed that in those capillaries which supply the muscles (organs peculiarly rich in potash-salts and phosphates) the largest number of blood-cells were destroyed; and that in the venous blood, which flowed from the corresponding parts (from the cephalic, external abdominal, digital, and median veins) there were far fewer blood-cells and a much smaller quantity of the phosphates and potash-salts than in the corresponding arterial blood or in the blood of other veins, which return the blood from other organs. These differences are so considerable, that in the venous blood of the muscles there are on an average from one-fourth to one-third fewer blood-cells than in the arterial blood, whilst in the blood of other veins the difference is either far smaller or there are relatively more cells (that is to say, absolutely less intercellular fluid).

We have already spoken (in vol. i, p. 361, and vol. ii, p. 310) of the doubt which still exists regarding the influence exerted by the presence of the fibrin on the plasticity of the exudations.

The present would be a fitting place to consider more attentively the more persistent exudations, and to investigate somewhat more circumstantially the chemical metamorphoses which run parallel with the morphological formations, but unfortunately this is a point on which we know little or nothing. As the solidifying parts of the exudation are far less accessible to chemical investigation than the fluid, our attention must of necessity be limited almost exclusively to the latter. I have made some attempts to ascertain the differences in the composition of the fluid which occurs in association with the solidified exudation, in so far as they are dependent on the metamorphoses which the original exudation has undergone. We know that these metamorphoses may be of three different kinds; in the first case, the exudation is gradually resolved,

and the coagulated fibrin slowly dissolved in the originally only slightly modified exudative fluid or in a serous fluid which is afterwards separated; in the second case, the solid part of the exudation hardens, ceases to swell in acetic acid, and becomes converted into a horn-like mass; and thirdly, the exudation is converted into true tissue, namely, connective tissue. One might suppose that the fluids remaining in these older exudations, or permeating the newly formed tissues, would exhibit differences which would readily admit of being chemically distinguished; but although these fluids certainly exhibit differences of composition on analysis, my observations at all events have failed to detect any definite constitution for any one special alteration of the exudation. We are still deficient in any more careful investigations for showing the character and composition of those forms of exudation, which tend towards the formation or regeneration of specific tissues (such as cartilaginous substance, osseous substance, &c.).

Croupous exudations. It is only in rare cases that we can succeed in subjecting to a chemical examination exudations of this kind whilst still in a perfectly fresh state, that is to say before they have been changed either by different metamorphoses which they have experienced during life, or by decomposition in the dead body. It may be shown with tolerable certainty that these exudations on their first separation are as fluid, and as similar to the blood-plasma as all other exudations; but they present this peculiarity, that when the fibrin has been coagulated, the fluid portion of the exudation is resorbed with such extreme rapidity that almost every effort to obtain it fails. It almost appears in the case of many of these exudations, as if only a kind of fibrinous juice had permeated the walls of the vessels, and had been deposited in a gelatinous form upon mucous or serous membranes. There is often scarcely a trace of blood-corpuscles to be detected in fibrin of this kind, and on rinsing the exudation with water, we obtain only a very small quantity of coagulable matter, and thus lose all hope of being able to ascertain the original composition of the exudation from the fluid enclosed in the coagulum. Then, moreover, it must be observed, that these coagula, or solid exudations, are in general formed gradually, and thus deposited in distinct strata, some of which experience greater alterations than others. However important it would be to ascertain the composition of these exudations immediately after their separation, the chemist is compelled to admit his entire inability to solve any of the questions which suggest themselves in connection with this point, and must direct his

attention almost exclusively to the solid parts of the exudations, which are always more or less altered.

Rokitansky, who would naturally judge of the nature of the depositions solely from their physical character, has arranged croupous exudations in three subdivisions,—a mode of division which has been much objected to, but which is undoubtedly recommended by experience, if we simply compare together facts under the most widely differing forms which they can assume, and exclude all those which merge into one another, as must be done in every artificial mode of division. A simple microscopical examination of these croupous exudations shows that the object which we are here considering is not pure fibrin, for even in the most recent formations the microscope reveals, in addition to a fibrous substance not very unlike freshly coagulated fibrin, a great number of molecular granules and flake-like laminæ, which at certain spots appear to be jagged. After they have existed for a longer time, we observe in them nuclei and cytoïd corpuscles; indeed the occurrence of the latter is often so sudden (or in other words the metamorphosis of the solid exudation into pus-corpuscles is so rapid) that many observers have altogether doubted the previous separation of fibrin. The questions which have been propounded to chemists since Rokitansky's original subdivision of the various kinds of fibrin, are in part solved by microscopical investigation. The substance to which Rokitansky applied the term croupous or aphthous fibrin, or which he regarded as the primary matrix differing from ordinary fibrin is now in a great measure found not to be fibrin at all; and he himself has noticed the absence of that network of fibres which is peculiar to coagulated fibrin both in the aphthous coagulum and in the croupous exudation β. These granular solid exudations are no longer fibrin, having undergone various chemical as well as morphological metamorphoses before they come under our notice. One might, indeed, here assume, as has been done, the existence of a dimorphism, such as has been shown in recent times to exist in the case of many mineral substances; but independently of the fact, that true heteromorphism is far less frequent in organic chemistry, and that its existence in respect to fibrin still remains undetermined, the qualitative chemical investigation of these exudations shows us that the granular matter which they contain is by no means chemically identical with the unaltered fibrin which is often still contained in these deposites.

In those exudations, which Rokitansky names *aphthous*, we find, after careful washing, no material which, after the exudation

has been digested for a short time in a dilute solution of nitre becomes dissolved and is coagulable or precipitable by acetic acid. (The washing is, however, by no means easy and frequently entirely fails, since the turbid fluid passing through the filter very soon closes its pores.) This insoluble residue swells up in a gelatinous form in very dilute hydrochloric acid; but some portion is actually dissolved, without, however, yielding the reactions of ordinary muscle-fibrin. A microscopical examination shows that the constituents of the very numerous cells contained in aphthous exudations are dissolved by water containing hydrochloric acid. Rokitansky's croupous exudation *a*, or fibrin *β*, contains true fibrin, in addition to the granular matter and the first stages of cell-formations; but although it is not very rich in blood-corpuscles, it is never entirely free from them. After an exudation of this kind has been comminuted and carefully washed with distilled water, and then immersed in a solution of nitre of the previously named concentration, at a temperature of 30° or 40°, a great portion of it is always dissolved, whilst the fluid is also found to contain a protein-substance, which is precipitable by heat at the boiling point, as well as by acetic acid; and here I must not omit to mention, that with the exception of two cases, I never found the so-called arterial fibrin (which is perfectly insoluble after digestion in a dilute solution of nitre), even in those exudations which according to microscopical examination appeared to contain true fibrin. The croupous exudation *a*, after being previously well washed in water, swells in dilute acetic acid; but a very small amount of the protein-substances, especially such as are recognisable by chromate of potash, are dissolved. Rokitansky drew attention to the large amount of *fat* contained in these exudations, and the fact may be readily confirmed by careful chemical analysis. The fat does not differ essentially from that of fibrin; but the fat containing phosphorus or rather the phosphate of glycerine appears to be present in rather larger quantities in the croupous exudation *a* than in exudation *β* or in the aphthous kind; but it must be admitted that there exists considerable uncertainty as to the quantitative determination of these substances. This observation seems to be confirmed by the fact, that these exudations on an average leave more *earthy phosphates*, and in general more acid phosphates, on the incineration of the constituents insoluble in water, than the ordinary blood-fibrin. I never found less than 2%, and often more than 4% of phosphates in the insoluble residue of the exudation.

Notwithstanding my conviction of the insufficiency of elementary

analyses for the examination of such substances, I have very frequently instituted analyses of this kind with the residue (insoluble in water, alcohol, and ether) of the croupous exudation of the first order (a); but the results were so variable, that it was impossible to compare them with the composition of the blood-fibrin. According to most of the analyses, the fibrin of the exudation contained somewhat less nitrogen than the fibrin of the blood of the same individual; and it was only once in seven cases that the nitrogen equalled the quantity found in the blood-fibrin. The quantity of carbon was equally variable, for in some cases I found rather more, sometimes from 1 to 2$\frac{0}{0}$ less, than in the blood-fibrin.

The croupous exudation of the second order (β Rokitansky) may be regarded as holding an intermediate place between that of the first and third order when considered in a chemical point of view. I have never found it to be perfectly free from pus-corpuscles.

Rokitansky distinguishes yet a third form of fibrinous exudation, namely, the *tuberculous*. Although in a purely physiological or even logical point of view, we can scarcely admit the assumption of such an exudation as a special form, its recognition is advantageous in a practical point of view. We entirely set aside the idea of an entirely specific process, and simply adhere to that which for ages has been attached to the term tubercles. In characterising this exudation, Rokitansky has here, as in other cases, not studied the original fresh product of the exudation, but only the peculiar form in which it most commonly comes under our notice. Persistence in a very low stage of development has in general been adduced as the most characteristic property of tuberculous exudations, and indeed we seldom meet with more than molecular granules, minute aggregations which have been regarded as of a special nature (tubercle-corpuscles), and, at most, faint indications of cellular structures. The absence of plasticity in these exudations has commonly been referred to the too rapid resorption of their fluid parts, and either to the actual absence of blood in the smaller vessels, or to other causes preventing these parts from being readily permeated with moisture. Where such a permeation as this takes place, we less commonly observe a formation of cells than of cytoïd corpuscles, which then give rise to what is termed softening of the tubercles. Tubercles have been divided, as is well known, in accordance with their form and mode of deposition, into miliary and infiltrated, and further subdivisions have been suggested, based upon their consistence and age (as for instance, gelatinously

infiltrated, cretified, &c.). On microscopic investigation, most of them are found to consist of fat-globules and molecular granules.

Notwithstanding the rapidity with which the tuberculous exudations are separated, and the circumstance that they are frequently secreted to the last moment of life in tuberculous patients, no attempts have as yet succeeded in obtaining for examination a perfectly fresh, still fluid exudation, of which one might presume with tolerable certainty that it would have been "tuberculised" had the life of the sufferer been prolonged. Even should these attempts succeed, it would still remain questionable whether the chemical investigation of these exudations would afford any further information regarding the so-called tuberculous process than has already been obtained from the analyses of the blood of tuberculous patients.

There is no exudation which, when once formed, admits more readily than the tuberculous of being studied with reference to the length of time which it has existed, and the various metamorphoses which it has undergone; thus we find on examining the lungs of persons who have died from chronic tuberculosis, that the most recent deposites are in the lower lobe, and the older formations in the upper one; but still the most careful and numerous micro-chemical and even microscopical investigations scarcely yield any reliable results, and the various micro-chemical analyses which I have made, in part conjointly with my friend Hasse, of the most varied pulmonary tubercles, have not yielded the slightest amount of scientific information. It would, therefore, be absurd to enter circumstantially into the details of these series of experiments, which are so frequently at variance with one another, although at the period when these analyses were made, many slight differences may have been passed over, which, in the present advanced state of animal chemistry, might perhaps have thrown some light on the subject; but still the results are so different, and even frequently so contradictory for entirely analogous objects, that no support can be obtained for even the most general mode of classification. We therefore withhold these details, trusting to future investigations for more satisfactory results.

The scattered facts yielded by works devoted to the subject may be limited to the following points. The tuberculous mass, when of recent date, contains, in addition to one of the protein-bodies, which is soluble with more or less facility in acetic acid and alkalies, a large quantity of fat, partly in very fine granules and partly in vesicles. In tubercles of longer existence the fat appears in much diminished quantities. The obsolete or cretified

tubercles consist chiefly of cholesterin, which may be recognised by the microscope, together with carbonate of lime, and a little phosphate of lime. The tubercles are generally deficient in salts, although the statements of authors on this point are as variable as the results which I obtained from my analyses of the different forms of these exudations. There is on an average more carbonate of lime in the ash of tubercles than in that of any other substance of the animal body which is rich in protein. The recent observation, that xantho-cystine occurs in old tubercles, is very remarkable, but I have not hitherto had any opportunity of verifying the correctness of this assertion. [See note to vol. i, p. 169, (on *xanthine*) in the Appendix.]

We must confess our inability to form a perfectly clear idea of Rokitansky's *albuminous exudations,* although we do not by any means believe that they can be classed under the same head as the purulent, or any other form of exudation. We have found that they presented very considerable chemical differences; and the turbidity which occasionally gives them a milk-white appearance is probably the simultaneous result of many different relations. The microscope shows that, in addition to the cellular elements, which occasionally become developed into spindle-shaped or caudate cells, there occur also a number of molecular granules, fat-globules, and a viscid filamentous substance, forming under the microscope hyaline stripes, and here and there probably also flakes of true fibrin. The turbidity arises in different cases from different microscopical elements.

This *filamentous matter* cannot, however, be regarded as true coagulated fibrin; for, independently of the circumstance that it cannot microscopically be confounded with ordinary fibrin, (since, like bronchial mucus, it acquires its filamentous appearance solely from the pushing or turning of the thin glass plate covering it, or from other mechanical conditions,) it differs completely from fibrin in the following chemical reactions. It commonly dissolves with considerable facility in solutions of neutral alkaline salts, when not too highly concentrated, without requiring any prolonged digestion or exposure to heat. Besides this, it frequently acquires a certain degree of opacity or milky turbidity, and is rendered less tough when exposed to the action of dilute acetic acid, dissolving only in an excess of this acid, or when it is concentrated; and, (excepting in two cases,) it has been found to dissolve easily in very dilute hydrochloric acid. The molecular granules occasionally consits of fat only, but they may frequently

be made to disappear by means of alkalies and akaline salts, on which account we may probably include them amongst the protein-bodies. We shall speak more fully at a future page of the micro-chemical relations of the other cellular structures which may occur in exudations of this kind. These fluids exhibit very different reactions; they are frequently so strongly alkaline and ammoniacal that one is disposed to refer their filamentous character to the strongly basic albuminate. The presence of the latter seems to be confirmed by the small quantity of coagulum which the fluid yields on the application of heat, while on evaporation a membrane is formed on the surface (see vol. i, p. 334). Dilute acetic acid frequently gives rise to a strong turbidity in such fluids, and occasionally to the separation of white flakes.

I have been unable to convince myself of the presence of true *casein* in such fluids either by the application of rennet or by other means; the viscid character and the reactions which these exudations exhibit are, therefore, probably owing to the presence of strongly basic albuminates. I have only on two occasions observed an acid reaction in these kinds of exudation (and this was after puerperal pyæmia), and here, also, acetic acid occasioned great turbidity in the filtered, opalescent fluid; the albumen coagulated into flakes when this exudation was boiled. The latter substance occurs, however, also in some cases when the fluid exhibits a faintly alkaline, or an almost neutral reaction (see above). In those cases in which the exudation has an acid or neutral reaction, the surface of the fluid, after the removal of the coagulated albumen, becomes covered on evaporation with a membrane, without, however, exhibiting the presence of true casein.

Notwithstanding the thick fluid character of these exudations, they seldom contain any large quantities of *non-volatile matters*, from 4 to 6% being the highest amount that I have found in these fluids. The amount of *fat* is not inconsiderable, although it frequently does not exceed the amount present in the normal, fibrinous, plastic exudations. The non-volatile *salts* are generally present in larger quantities than in the blood, but on comparing them with the salts of the plastic exudations, taking the solid residue as the unit, the number representing the salts is often higher in the fibrinous than in the albuminous exudations. Although it was found from a comparison of the salts as given by several analyses, that there was a relatively smaller amount of the phosphates in the albuminous than in the fibrinous exudations, this observation requires to be further corroborated; the more so,

because I found in two cases (in puerperal fever with pyæmia) considerably more phosphates than one usually meets with in the salts of the exudations. The occurrence of large quantities of bile-pigment and biliary acids, urea, sugar, &c., in certain albuminous exudations must be regarded as purely accidental, and as admitting of an easy explanation in individual cases.

Rokitansky's *serous dropsical exudations* coincide perfectly with the *transudations* which we treated of in vol. ii, pp. 308-331, but we think we have sufficiently explained, both there and in the introduction to the present section, the reasons which compel us to separate the transudations from the exudations. No one can deny that in some cases an exudation may become associated with a transudation, or, conversely, a transudation may associate itself with an exudation, but the two processes must in principle be widely distinguished, as, in fact, they do occur distinct from each other in most cases, leaving no grounds for confounding one with the other. The erroneous idea that the plasticity of an exudation depends only upon the quantity of fibrin which it contains, has led many persons to doubt the propriety of separating exudations from transudations, as we meet with plastic exudations without fibrin, and non-plastic ones which contain fibrin; but we think we have satisfactorily shown from our own direct investigations, that the plasticity of the exudations is constantly associated with the presence of a certain amount of soluble phosphates, which occur either in very small quantities or are even wholly wanting in the transudations. As the phosphates and potash-salts can originate only in the blood-cells, they cannot occur in large quantities in the exudations, or render the transuded liquor sanguinis plastic, unless there is true stasis and destruction of the blood-corpuscles, when the contents of the latter transude through the lacerated or uninjured walls of the capillaries. The formation of transudations poor in phosphates and potash-salts, is solely dependent on a retarding of the blood-current in the capillaries and on other mechanical relations, and in no case depends upon a complete stasis or destruction of the blood-corpuscles,—in other words, it never depends upon true inflammation.

We do not, however, by any means incline to the view, that the plasticity of an exudation is solely owing to the presence of phosphates (although their influence on the formation of the tissues in the case of animals, has been almost demonstrated by direct observation); it is, on the other hand, very probable that other substances may constitute essential requirements for pro-

ducing plasticity, although these, like the former, would appear from the results of our investigations to derive their original source from the blood-corpuscles. To assert that the plasticity of an exudation depends solely upon the presence of the phosphates, would be no less unsuitable or uncalled for, than to assume that transudations owe their origin exclusively to a large amount of water in the blood. We have already shown, under the head of "Transudations," the untenable nature of such a view, and we would here only remark that the blood of tuberculous, chlorotic, and hysterical patients is often found to be far more watery, without, however, transudations having taken place, than the blood of patients having dropsical accumulations in different cavities. We have already instanced amongst the conditions which favour the formation of a transudation, the amount of the lateral pressure exerted by the blood on the walls of the capillaries, the rapidity of the blood-current, the coefficient of elasticity of the walls, and many chemical relations. We cannot, however, venture here, any more than in the involved phenomena of vital processes generally, to refer an important process to one single, perhaps accidentally induced condition; for, in adopting such an unsatisfactory mode of evading a difficulty, we should run the risk of falling into the error which is too common amongst physicians of the present day, of referring the most complicated pathological processes to the merest chimeras, and endeavouring to explain the *modus operandi* of certain powerful or inefficient remedial agents by clumsy mechanical or chemical hypotheses.

The *purulent* and *ichorous exudations* show in special cases the same amount of affinity with the albuminous, and in part even with croupous exudations, as do the other exudative processes. In its purest state the purulent exudation generally, however, forms a yellowish, thick fluid, which differs from every other exudation by the considerable amount of corpuscles which are distributed through it with tolerable regularity.

These corpuscles, which, however, also occur in other places and in other fluids, as, for instance, in the lymph (as lymph-corpuscles), in the blood (as colourless blood-cells), in the mucus of the mucous membranes (as mucus-corpuscles), &c., are, as is well known, vesicles consisting of a cell-membrane, which often appears granular, of viscid hyaline contents, and of a nucleus which adheres to the cell-membrane. These corpuscles may or may not be included under the head of cells, according to the idea entertained of the physiological cell; and on this account it would

be desirable, perhaps, to avoid the numerous designations which have been applied to these bodies, and to adopt the name of *cytoïd corpuscles* proposed by Henle (*F.* P. 11, F. 3).

We do not purpose entering more deeply into the morphology of pus, its mode of formation, &c., as this would be leading us too far from the main subject of our inquiries, and involving us in a labyrinth of unanswered or unanswerable questions and the vaguest conjectures, as the chemical investigations hitherto made in this department of inquiry have contributed very little towards the elucidation of pus and purulent exudations. Although we found ourselves compelled on a previous occasion, when investigating the micro-chemical characters of pus and suppuration,* to hazard various hypotheses on the morphological as well as the chemical nature of purulent formations, we are nevertheless of opinion that where chemistry is not sufficient in itself to solve the difficulties falling within its own scope of inquiry, it ought not to assume the semblance of being able to lay the foundation of a rational enquiry by the aid of unstable conjectures and mere assumptions—the imputation of which has, on too many occasions, clung to this science. We will not, therefore, enter further into the genesis of pus-cells, or of the morphological elements allied to them, nor will we dwell on the physiological value of these cells, the different characters of laudable and malignant pus, &c., as almost every recent histological and pathological work abounds in the most comprehensive facts and opinions bearing upon these points. The sifting of the chemical facts before us will also be a matter of extreme facility, owing to the very small number of positive results yielded by the earlier chemical investigations.

The reason why a very subordinate degree of interest attaches itself to the earlier investigations made on this subject, many of which were conducted with great care, depends in a great degree upon the difficulty, or even impossibility, of separating the cytoïd corpuscles of the pus from the intercellular fluid, (the so-called pus-serum,) although such a separation is obviously necessary to afford such a view of the constitution of the pus, as may at once accord with nature and satisfy the requirements of physiology. A quantitative determination of the constituents of the corpuscles, such as we have at all events approximately obtained for the blood, is scarcely possible as yet in the case of pus. Pus-corpuscles do not admit more readily than the blood-corpuscles of being

* Arch. f. phys. Heilk. Bd. 1, S. 218-265 [a joint memoir by Lehmann and Messerschmidt.]

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separated by filtration from the intercellular fluid, and they also render indirect determination more difficult, in consequence of their possessing a far less sinking capacity than the blood-corpuscles; the cytoïd corpuscles of the blood remain, however, suspended like those of pus. After standing for some time, the pus-corpuscles begin gradually to sink; the pus is then, however, generally changed in character, and the cytoïd corpuscles exhibit more distinctly the nuclei which had previously been scarcely discernible. The serum of the pus has a less decided alkaline reaction than that of the blood; indeed sometimes it is acid, and when placed in a vacuum, this kind of pus commonly evolves sulphuretted hydrogen gas. We cannot, therefore, regard the serum of the pus, which is accessible to investigation, as a perfectly pure object. But although this condition of the pus-corpuscles must be regarded as the principal obstacle in the way of a rational investigation of this fluid, there are not wanting other causes which very frequently render the object unsuited for a conclusive analysis; amongst these we may especially enumerate the frequent occurrence of blood in pus, that is to say, particles of fibrin and blood-corpuscles, as well as the elements of newly formed, or recently destroyed tissues. Such fluids would, at all events, be unsuited for analyses, from which we might wish to draw conclusions regarding the special character of the pus, and of the purulent exudations generally. Another circumstance which calls for attention is, that to render an analysis of the pus thoroughly useful, it is essential to institute simultaneously an analysis of the blood; yet what physician would be so unconscionable as to prescribe venesection in the case of a patient in whom the purulent discharge was so copious as to afford the chemist sufficient materials for a proper analysis? We must, therefore, necessarily content ourselves with having recourse to the lower animals for this purpose. There is nothing of chemical pedantry in desiring parallel analyses of the blood, but yet the accuracy of a physico-scientific inquiry would not be invalidated by its omission. It is obvious that the constitution of the pus must in a great degree be dependent on that of the blood, and that an accurate examination of the former must embrace a notice of the character of the blood also; but one would hardly believe that this influence could extend so far as to manifest itself in the physical character of the corpuscles; yet it is by no means difficult, after some little practice, to determine from the form, size, granulation, &c., of the corpuscles, the nature of the source from which they have originated.

Thus, for instance, the pus from accidental wounds or ulcerated parts in a phthisical patient presents under the microscope a totally different appearance from that of a typhous subject, whilst that of the latter would in its turn differ essentially from the appearance presented by the pus taken from a drunkard or from a patient exhibiting the cancerous dyscrasia; and this would be observable even in cases in which the suppurative fluids could not be regarded as the ordinary ichor of surgeons. In case these observations should excite a doubt in the minds of those who have been accustomed to examine pus under the microscope, we would simply refer to the fact that the mere size of the linear diameter of a cytoïd corpuscle frequently furnishes a clue to the nature of the fluid from which it was obtained; thus, for instance, Henle* found that the cytoïd corpuscles in the pus measured on an average from 0·004 to 0·005‴, that those in the saliva and mucus were somewhat larger, and those in the blood were, on an average, smaller. These differences he ascribes, undoubtedly with much truth, to the different densities of those fluids. When therefore we find that the mere density of the blood, on which depends that of almost all the other juices of the animal body, exerts so great an influence, we can scarcely suppose that the other qualities of the blood should exercise no action whatever on the chemical constitution of the pus. We can hardly therefore be accused of adopting any exaggerated or far-fetched view if we regard all analyses of pus, which are unaccompanied by simultaneous analyses of the blood, as devoid of all importance in interpreting a physiological process, or in promoting the recognition of the true constitution of normal pus. We have deemed it expedient to make these preliminary remarks, partly to free ourselves from the reproach of having neglected the laborious investigations of former inquirers in our representation of the chemical relations of pus, and partly to prevent, as far as lies in our power, the misapplication of efforts which would be lost to scientific pathology, by being expended on the chemical analysis of objects whose examination can in no way promote the advance of science.

We have already observed, in reference to the plasma or the germinal fluid of the pus, that it appears to be originally identical with the fresh plastic exudation which we examined from the secretion of a wound. We will here subjoin a few remarks in addition to the relations which we have already described. In one case the secretion was collected from wounds which had been

* Handb. der ration. Pathol. Bd. 2, S. 685.

inflicted upon eight rabbits in the manner already described: as soon as it began to flow free from blood-corpuscles, 100 parts of the solid residue contained (as was determined by direct incineration) 12·341 of mineral substances (the solid residue of the serum and of the fibrin yielding 9·971%); 100 parts of the salts of the secretion from the wounds yielded 41·145 parts of chlorine, 5·819 of phosphoric acid, and 6·941 of potash, whilst from that of the liquor sanguinis there were obtained 53·145% of chlorine, 2·014% of phosphoric acid, and 4·814% of potash. In the solid residue of the secretions from the wounds in three geese there were 15·148% of mineral substances (in that of the liquor sanguinis there were 11·155%); 100 parts of the salts of the wound-secretion contained 7·018 of phosphoric acid and 7·147 of potash, whilst in those of the corresponding liquor sanguinis there were 3·118 of phosphoric acid and 4·663 of potash. Several experiments of a similar nature, conducted by my pupils, yielded analogous results. It has already been observed that the secretion from a wound does not long retain the character of a fresh exudation, but that it soon exhibits morphological elements, molecular granules, nuclei, and even cytoïd corpuscles, when the edges of the wound do not cohere, that is to say, when the wound does not heal *per primam intentionem*. It may therefore be assumed that the exudation, as soon as it has become pus, will exhibit a different composition from the fresh wound-secretion, which may be able to produce tissue, but cannot generate abortive cells (that is to say, pus-corpuscles). A similar mode of reasoning has led to the assumption that the first secretion from a wound which is free from blood may perhaps contain a sufficient quantity of phosphates and potash-salts to restore the integrity of the injured tissue, whilst the later secretion very probably contains only enough salts to form cytoïd corpuscles, but not a supply adequate for the formation of perfect cells or fibres. It happens very frequently, however, that the idea we have been led to entertain of the plan adopted by nature does not coincide with actual observation. At all events, the limited experiments which I have been able to make, and which were restricted to rabbits, do not confirm such assumptions. The ash of pus always contains a larger amount of phosphates and potash-salts than the intercellular fluid of the corresponding blood, although when compared with that of the fresh secretion from a wound it exhibited a very variable amount of these salts. This relation, which requires to be confirmed by further observations, can scarcely excite surprise, for there is undoubtedly something

more necessary than phosphates and potash-salts to render an exudation truly plastic.

Without entering further into the consideration of the incidental morphological constituents of pus, we will at once proceed to its cytoïd corpuscles. On micro-chemical investigation they present the following reactions. (*F.* P. 11, F. 3 and 4).

If fresh pus be very much diluted with distilled *water*, the corpuscles are seen to swell and become very pale; the granular character of their surfaces either wholly disappears or true granules become detached therefrom. The interior of the corpuscles occasionally exhibits a distinct nucleus, but more frequently only an aggregation of granular matter with no distinct outlines, whilst in addition to this, the corpuscles also exhibit in their interior fine granules, which are in a state of active molecular motion. Henle has especially called attention to the circumstance that, on the addition of water, some of the pus-corpuscles burst, and allow their viscid contents to escape, which then become dissolved in the dilute serum. The corpuscles then appear collapsed, are much darker, and still contain nuclei. The action of the water is best observed in the cytoïd corpuscles of the buccal mucous membrane; the lenticular nucleus, which may be here very readily recognised, is generally simple, that is to say, not cleft, and is then situated so close to the investing membrane of the corpuscle that it frequently appears as if it were attached to this membrane on the outside of the cell. This nucleus is brought more prominently into view on the addition of water, which does not cause it to split.

Strong *alcohol* causes the serum of the pus to coagulate, and hence renders a microscopical examination of the corpuscle unavailing. But when spirit containing 23% of alcohol is employed, which induces no turbidity of the pus-serum, the corpuscles appear distorted, somewhat elongated, and, as it were, caudate or pointed.

In *ether*, free from alcohol, the corpuscles are also distorted.

When fresh pus is treated with very *dilute mineral acids*, as hydrochloric acid (1 part in 2,800 parts of water), nitric acid (1 part of anhydrous acid in 2,000 parts of water), phosphoric acid (1 part in 1,500 parts), or tolerably dilute *organic acids*, as acetic, lactic, oxalic, tartaric, racemic, or citric acids, no coagulation takes place, but the pus-corpuscles swell to so great a degree that they frequently attain double their original size. The granular appearance, which may very probably have been owing to plaits in the capsule, disappears; the latter, which appears to be extremely

hyaline, very often bursts, when its torn and ragged fragments may be distinguished at different points, provided the light is good and the diaphragm be judiciously employed. Where the nucleus was originally visible, and of a simple, lenticular form, it retained this appearance after the action of these fluids; but in those cases in which it had originally been invisible, or where its appearance could only be detected by a darker spot in the corpuscle, the nucleus was generally tripartite and had a sharply defined outline. One or two dark granules may often be observed in or upon the nuclei, but we leave it to the physiologists to decide whether they should be regarded as nucleoli.

Concentrated mineral acids coagulate the protein-bodies, and hence the distorted corpuscles cannot be distinctly recognised amongst the separated granules of albumen. The organic acids act in the concentrated state in much the same way as when diluted, causing the variously cleft nuclei to appear perfectly distinct, although their different parts cohere together.

The caustic alkalies, if used in a moderate degree of solution, exert a rapidly destructive action on the cytoïd corpuscles; perfect solution never takes place, but after having continued for some time visible, the corpuscles disappear on the addition of water, leaving only a gelatinous-like residue, in which various lighter and darker points may be recognised. Dilute alkalies destroy the corpuscles even more rapidly than the concentrated solutions.

Aqueous solutions of *neutral alkaline salts* cause the sharp edges of the pus-corpuscles to disappear rapidly, contracting the latter until they appear smaller, granular, and jagged,—an effect which is probably to be referred solely to endosmotic action; the fluid contents are discharged into the serum; the capsule then becomes plicated, and consequently assumes a granular appearance, which prevents the nucleus from being seen, although it may previously have been visible.

Solutions of *alkaline carbonates or borates* also contract and distort the corpuscles; their prolonged action produces the same results as caustic alkalies, for without having previously rendered the nucleus visible, they gradually dissolve the corpuscles, leaving only some few granules, which are held together by a tough hyaline substance.

If pus, in which the nuclei of the corpuscles have been rendered visible by *dilute acids,* be treated with solutions of *neutral alkaline salts,* the previously distended capsule contracts, and the nucleus becomes invisible, whilst the whole corpuscle is much distorted.

But, conversely, if we add an extremely dilute mineral acid to pus which has been mixed with such a saline solution, it rarely happens that we can again render the nucleus visible. On this account we can rarely detect the presence of nuclei in the cytoïd corpuscles of the urine in catarrh of the bladder by means of a dilute acid.

An aqueous *solution of iodine* (1 part of iodine in 9,000 parts of water), containing a trace of hydriodic acid, does not coagulate the serum of the pus, but it imparts a yellow colour to the corpuscles, causes them to swell, and brings the nuclei more prominently into view. A concentrated solution of iodine (whether the concentration be effected by chloride of sodium, spirit, or hydriodic acid) coagulates the serum of the pus, and brings into view the nuclei of the corpuscles which are not entirely concealed by the coagulated albumen.

Whatever evidence these micro-chemical experiments may afford on the question of endosmosis, they throw very little light on the internal chemical nature of the pus-corpuscles, and scarcely even indicate the direction we ought to follow in rendering the separate morphological constituents of the cytoïd corpuscles accessible to more exact chemical inquiry. This much only seems clearly established, namely, that the investing membrane, the viscid contents, and the nuclei, are substances very closely allied to albumen; nearly all of them exhibiting the reactions peculiar to the protein-bodies. The *investing membrane* is a protein-body, which does not merely swell in a gelatinous manner in very dilute acids, but actually dissolves in these fluids. This property, which it exhibits in common with albumen and muscle-fibrin, distinguishes it very decidedly from blood-fibrin, which swells up, but does not dissolve in dilute hydrochloric acid. This membrane is wholly insoluble in alkaline salts, and does not dissolve readily even in the caustic alkalies. These properties very strongly exhibit the points which mainly distinguish it from neutral albumen which is poor in salts (such, for instance, as the albumen obtained from an alkaline solution by neutralisation with acetic acid and by excessive dilution, or by the careful addition of dilute spirit,) or from casein which has been freed from salt and acid (according to Bopp's mode of exhibition), whilst its behaviour towards the caustic alkalies and their carbonates and borates makes it approximate more nearly to muscle-fibrin (syntonin). If the serum of the pus and the viscid contents of the corpuscles admitted of being removed, the most practicable method would

appear to be that of dissolving the cell-wall in water containing hydrochloric acid, and exhibiting the matrix in a similar manner as with muscle-fibrin; but this apparently practicable method of dilution with water and decantation, which, according to the above reactions, indicates no difficulties at the first glance, is found to fail most entirely on being tried, and we are still ignorant of any other method of removing the serum of the pus, without dissolving the investing membrane.

It may appear a very simple matter to isolate the *substance of the nuclei*, but even in this respect our expectations are not realised, for when we attempt to dissolve the cell-walls by means of dilute mineral acids or concentrated solutions of organic acids, we are scarcely ever able to succeed in completely dissolving the capsules of all the corpuscles, whilst, moreover, some portion of the viscid contents always remains undissolved in the form of fine molecules, which cannot altogether be regarded as fat, since they cannot be made to disappear when treated with ether. The great difficulty of obtaining the nuclei in a pure state consists, however, in the complete impossibility of separating the undissolved particles by filtration or decanting. When treated with concentrated nitric or sulphuric acid, or with chromic acid, the material of the nuclei exhibits reactions, which seem to place it in the group of the protein-bodies, whilst the difficulty of its solution in concentrated alkalies, and the facility with which it dissolves in dilute caustic alkalies even more rapidly than the cell-walls, seem rather to show that this substance possesses considerable affinity with the nuclei of the cells of the horny tissue.

We are unable to decide anything regarding the chemical nature of the nucleoli, for when the cytoïd corpuscles are digested with dilute alkalies till their distinctive character can no longer be recognised, there remain, as we have already observed, more or less deeply tinged molecules, among which the nucleoli may possibly be present. On treating these masses with ether, a portion of the punctated mass disappears, but individual granules are still visible. But we are unable to decide whether these are the remains of the granules which were previously visible, or whether they have been separated by the ether; and hence we do not know whether the original molecular granules consist entirely or only in part of fine fat-granules. If we treat the nuclei, which have been obtained from pus by digestion with acetic acid and subsequent decantation (as far as this is practicable,) with a not too dilute solution of potash, we find that there is formed, on

heating, a gelatinous mass almost insoluble in water. This substance, which was formerly believed to be the matrix of the nucleoli, and held to be a special material allied to horny substance (keratin), has been as yet found to present no differences from the strongly basic albuminates of potash, to one of which we have already referred in vol. i., p. 333. Other protein-bodies, moreover, besides albumen, enter into similar gelatinous combinations with potash, and, like them, do not very readily dissolve in water. A great number of the substances which have been pronounced to be *keratin*, are nothing more than compounds of strongly alkaline bases with protein-bodies.

In the experiments on pus made by Messerschmidt and myself, to which I have already referred, we were lead from certain reactions to the erroneous conclusion, that we had been able to distinguish several varieties of fibrin in the capsule, nuclei, and nucleoli, an error which, unfortunately, met with more general approval than it deserved, considering the state of science at the time. We believe that we have now shown that there are not sufficient grounds for regarding any constituents of the pus-corpuscles as identical with fibrin, and we need scarcely repeat the remark we have so often made, that it is injurious to the cause of science to attempt to identify or name different substances without having had the power of closely investigating them. A deficiency in our knowledge is in such a case very far preferable to the mere accumulation of vague hypotheses.

We have already shown from direct observation (vol. i, p. 252) that *fat* is accumulated in the corpuscles of the pus.

We are, unfortunately, still deficient in observations which would enable us to judge of the quantity of *salts* contained in the pus-corpuscles when compared with the amount present in its serum.

We now proceed to consider the constituents of the *serum of the pus*. This fluid, when we can succeed in skimming it from the corpuscles, which only sink very slowly, is found to be entirely colourless, or of a faint yellow colour, and perfectly clear; it rarely contains fat-globules; it has a faintly alkaline reaction, and coagulates on being heated, most frequently into flakes, but sometimes in the form of a dense white mass. Acetic acid occasionally renders it strongly turbid.

The *albumen* of the intercellular fluid of the pus does not differ from that of the blood; at all events, all its reactions correspond perfectly with those of ordinary albumen. Moreover, the quantity

of albumen in the serum of the pus is very variable, according to the source from whence it is derived; in the four analyses which I was alone able to make, I found from 1·2 to 3·7% of albumen in the serum of the pus of different persons.

Mucin is not present in pus, except the latter has been obtained from inflamed mucous membranes; it may in general be easily distinguished by a microscopical examination of the precipitate from other substances, which are precipitable by acetic acid. It presents an appearance of whitish striped flakes or membranes (see vol. ii, p. 371).

Pyin is a substance which is in like manner precipitable by acetic acid, although it differs from mucin as much as from casein. This substance which was first shown by Güterbock* to be present in pus, is not of constant occurrence; it is certainly absent from the pus of wounds in healthy persons. Güterbock obtained it from the pus by coagulating the latter with alcohol, and extracting the residue with water; it is remarkable for being precipitable with acetic acid and a solution of alum, whilst it remains perfectly undissolved in both these fluids. Notwithstanding the frequent notices of this substance in works treating of pus and mucus, it has been very imperfectly investigated. Mistakes may, however, easily be made; thus, for instance, on coagulating the pus, the fluid becomes more strongly alkaline; the alkali dissolves a portion of the coagulated albumen, and this solution, when acted upon by acetic acid, deposits a considerable precipitate, but this latter does not dissolve in an excess of acetic acid as rapidly as one might have been led to expect from the assertions of most writers. A mistake may, therefore, easily occur even when the absence of mucus or casein can be demonstrated; the latter point is not very easy of proof, except in some special cases. Scherer† has submitted pyin-like bodies to elementary analysis, and in the course of these observations he found that what had been regarded as a simple substance, and supposed to be pyin, consists in fact of very various substances with the most different composition. Many persons have considered pyin to be an oxide of protein, indeed, as Mulder's tritoxide of protein; but it will be found on a closer examination that the reactions of pyin do not correspond better with this substance than Scherer's elementary analyses of the latter do with Múlder's analysis of the tritoxide. Many authors are of opinion that pyin may be a transition-stage from fibrin to gelatigenous

* De puris naturâ et formatione; diss. inaug. Berol. 1837.

† Untersuchungen zur Pathologie, S. 85-96.

tissue, or a product of fibrin entering into a state of suppuration; but these conjectures have not hitherto been confirmed by the positions in which this substance occurs, so far as they have yet been accurately observed, or by its chemical reactions.

Scherer has submitted to elementary analysis several specimens of pyin obtained from different exudations, and has found that their composition was almost precisely the same as that of protein; however, he also found other constituents of the exudations which appeared very similar to pyin, but differed very much from it in composition, being especially remarkable for their abundance of nitrogen (= 22·37%).

Casein does not occur in normal pus, and its presence has not been proved with certainty even in abnormal forms of the secretion. The deficiency of our knowledge of the protein-bodies and their immediate derivatives is nowhere more forcibly shown than in the investigation of pathological products.

The quantity of *fat* in pus, the occurrence of which has been regarded as highly characteristic, differs extremely according to the source from whence it is derived; although, when compared with the amount contained in many other fluids, it is rather large. It is very considerable, and is always present in all abscesses of the mammæ; cancer of the breast, however, always exhibits a larger amount of fat than any other carcinomatous growth. In ordinary pus the quantity of fat varies, according to our observations, which agree with those of Güterbock, Valentin,* and von Bibra,† from 2 to 6%. The different fats seem to consist of olein and margarin, alkaline oleates and margarates, and variable quantities of cholesterin. We cannot entirely admit the correctness of Simon's view, who held that the fat-globules which appear on the addition of acetic acid to pus, consist principally of liberated fat derived from the corpuscles, since it may also be dependent on the decomposition of the *soaps* dissolved in the pus-serum; and, indeed, fat-globules are often perceived in pus-serum after it has been treated for some time with acetic acid, which were previously not to be perceived. Pus occasionally contains a tolerably large amount of *cholesterin*, and Valentin found as much as 1% of this substance in pus which had been taken from an abscess in the thigh. On a careful examination of the masses of fat extracted with hot alcohol and ether from the residue of the pus, a little fat containing phos-

* Valentin's Repert. 1838, S. 307.

† Chem. Untersuch. verschiedener Eiterarten u. s. w. Berlin, 1842.

phorus may always be detected in the residue which is insoluble in cold ether.

Normal pus generally contains from 14 to 16% of *solid constituents.* The purulent exudations which occur in serous cavities and bad ichorous pus, often contain a smaller amount of solid constitutents. These solid matters contain from 5 to 6% of mineral or inorganic substances in the pus of healthy persons, whilst the amount may rise to 10 or even 14% in bad pus and in watery transudations. The ratio of the insoluble to the soluble salts in healthy pus varies from 1 : 7 to 1 : 9, whilst in bad pus it often = 1 : 15 or even 23. It follows from these observations, that in bad pus a greater or smaller quantity of simple transudation must have become mixed with the true plasma of the pus.

The *insoluble salts* of pus are those which usually accompany the protein-bodies, namely, the phosphates of lime and magnesia, in addition to which there is always a variable amount of carbonate and sulphate of lime generated by the process of incineration. There is, moreover, always some oxide of iron to be detected in the ash of pus, even when no trace of blood-corpuscles is to be discovered in the fresh fluid.

Chloride of sodium constitutes the principal part of the *soluble salts* of pus. H. Nasse long since drew attention to the fact that the serum of the pus and its solid residue contained three times more of this substance than the blood-serum and its solid residue; and even when the quantity of the chloride of sodium of the whole pus is compared with that of the blood-serum, the former is always found to be the larger. A comparison between the chloride of sodium in the serum of the pus, and that which is present in pus rich in corpucles, shows that here, as well as in the blood, the larger proportion of this salt is dissolved in the intercellular fluid, and that a very small quantity only is contained in the pus-corpuscles.

The ash of the pus does not contain a very large amount of *soluble phosphates,* but, as we have already stated, no approximate estimate or definite relation can be established between these and the other salts. The quantity of soluble phosphates in the ash of different kinds of pus varied between 3 and 10%. Moreover, the quantity of potash in the different kinds of pus did not admit of being definitely determined; this much only was constantly observed, that there was always more potash present than in the intercellular fluid of the blood. The experiments made on the pus of rabbits did not lead to any more definite results.

I succeeded by the same methods which I employed in the

case of the blood and the transudations, to show the presence of *alkaline carbonates* and *free carbonic acid* in the pus.

In the pus, as in almost all other exudations, we meet with *bile-pigment*, the *biliary acids*, *urea*, and *sugar*, as incidental constituents.

Glycocholate and taurocholate of soda were found by one of my pupils in pus from a large abscess in the thigh of a patient with catarrhal icterus; another pupil found sugar in the purulent discharge yielded by the blistered surface of a patient with diabetes.

We may conclude with the supplementary remark, that morphological elements which do not, strictly speaking, pertain to pus, are sometimes found in it; amongst these we must reckon the fibrinous coagula which are often met with in suppurative exudations when they liquify into pus (pneumonic sputa). In the pus of old abscesses, and in the ichorous discharge from ulcers, we very often find crystals of phosphate of magnesia and ammonia, not unfrequently vibriones, and sometimes microscopical fungi and confervæ.

Acid pus is probably of very rare occurrence in the animal body; when pus has continued stagnant for a considerable time in the cavity of an abscess (in what are termed cold or congestive abscesses), it very generally undergoes alkaline fermentation; it then contains some *carbonate of ammonia* and triple phosphate, besides a large amount of *sulphide of ammonium*. I have only found the purulent exudations present in some few cases in empyema. Phthisical patients sometimes expectorate sputa having an acid reaction, although no acid substance had come in contact with the expectorated matters, either whilst they were passing through the mouth or after they were thrown up. The rare occurrence of acid pus is the more remarkable, as it very rapidly turns sour on being left in imperfectly closed vessels. When healthy pus is suffered to remain for several days in a corked bottle containing a certain amount of air, and exposed to a summer temperature, we find on examining it under the microscope, that the corpuscles have swelled and become more transparent, whilst the fissured nuclei are also speedily brought more distinctly into view; after a longer time the reaction is decidedly acid; numerous isolated nuclei without a trace of cell-walls, and some few perfect corpuscles, are seen under the microscope, and interspersed amongst the corpuscles and the nuclei are innumerable molecular granules, whilst here and there we may detect tablets of cholesterin and a confused

mass of threads of margarin. After pus has continued standing for several months, the different fats appear in the most beautiful forms, such as no artificial means are able to produce. Even with the naked eye we may detect white granules here and there in the pus; these granules consist partly of a confused mass of fine threads of margarin, but chiefly of ensiform, lily-leaf-shaped, variously contorted and intersecting bundles of crystals of margaric acid, in which are embedded separate groups of tablets of cholesterin. (*F.* P. 11, F. 5).

The distinctions between pus and mucus, which so largely attracted the attention of the physicians of an earlier day, have lost all their supposed importance, since modern physiology has shown that the two fluids are separated only by the most gradual transitions, and that the mucus in inflammatory affections of the mucous membrane gradually presents large numbers of cytoïd corpuscles, together with albumen, and thus acquires great similarity, if not a perfect identity with pus, both in respect to its physical and chemical characters. Even the quantity of fat in the purulent fluid secreted by the mucous membrane in a state of inflammation, is very often fully equal to that of genuine pus, a fact to which Güterbock attached great diagnostic value. The pus of the mucous membranes commonly retains the property possessed by mucus of gelatinising on the addition of water or acetic acid.

Rokitansky's *ichorous exudations* constitute an ill-defined group, corresponding in many particulars with albuminous exudations. Their chemical properties differ as much as their physical characters; many are also entirely inaccessible to chemical investigation, which would, moreover, be wholly useless, as they frequently are nothing more than simple products of putrefaction, and the detritus of the dead (gangrenous) tissue.

In like manner we cannot ascribe the acid reaction, which is more frequently observed in these than in other exudations, to an organico-vital process; nor do the scanty chemical investigations which we possess afford the slightest insight into the true source of the irritating character of many of these exudations, more especially of those which were originally coagulable, and deposited clots of fibrin.

Rokitansky's *hæmorrhagic exudations* are even less amenable to chemical inquiry, and do not, therefore, fall within the scope of the present work, since they can only be considered from a purely anatomical point.

The hæmorrhagic exudations lead us to the consideration

of the metamorphoses which the blood undergoes when it stagnates in vessels which have become occluded (in thrombus), or is effused in individual tissues (as in extravasions and apoplectic centres). Many of the most distinguished inquirers have made this question the subject of the most careful investigations; the morphological metamorphoses which occur in such sanguineous extravasations have been observed under the microscope, from their earliest origin to their persistent condition at a certain stage of development, or to their final disappearance; yet, notwithstanding all these researches, many of the points already observed remain obscure and wholly inexplicable, the different opinions of inquirers being here more entirely at variance with one another than in any other department in the history of development. The chemical history of these exudations is still more deficient, for here we have actually no observations. Histologists have endeavoured by the aid of certain micro-chemical means to throw some light on this obscure subject; but these attempts have either been of no avail whatever, or have yielded very doubtful results, —an apparently similar structure behaving differently in different cases under the same reagents. A similar remark may be made in reference to the development of pathological exudations into those abnormal cellular masses which especially characterise cancerous structures, or into those fibrous tissues which we meet with in fibroid tumours. Many young physicists, despairing of the possibility of explaining these matters, and the processes on which they depend, by chemical means, have probably shared with us in the sanguine expectation that histology, which had already thrown so much light on the development of normal tissues, would aid our chemical researches; but in these expectations we have demanded more than chemistry is able to accomplish, whilst we have also probably underrated the extreme diversity of these highly complicated vital processes.

ZOOCHEMICAL PROCESSES.

After having traversed the extensive domain of the organic substrata, which serve as the solid basis of the zoo-vital processes, and endeavoured, in accordance with the principles of an enlightened physical inquiry, to form a correct estimate of the chemical and physiological value of the numerous members of those groups of atoms which serve the animal body both as materials for its structure, and as the means by which its movements are effected, we at length approach the special aim of our inquiries, namely, the study of the phenomena manifested during life in those parts of the animal organism which we have been considering, and the elucidation of the internal connection existing between such diversified phenomena and the causes on which they depend. We drew attention in the introduction to the present work (see vol. i, p. 13) to the maxims and principles which ought to guide us in our attempt to unravel the hidden processes of material life; we will not, therefore, enlarge upon our previous remarks, or expatiate any further upon a subject which has been treated with so much more ability by other writers, as, for instance, by Lotze* and John Stuart Mill.† Yet, when we take a survey of the collective mass of positive facts, we find a mere accumulation of disjointed fragments, the natural connection of which we are rarely able to discover, since we often lack the intervening links by which alone we should be enabled to follow the endless chain of vital phenomena. A careful study of the material substrata of animal life, as far as the present condition of science admits of such an investigation, cannot fail to show us how far removed we still are from obtaining a scientific basis for a true inductive treatment of the material processes of life; and, indeed, it would almost seem to require the marvellous powers of combination of a

* Allgem. Physiologie des körperlichen Lebens. Leipz. 1851.

† A System of Logic, rationative and inductive. London, 1843.

Liebig to collect together and combine into a connected whole the scattered threads which constitute the materials for the study of the metamorphoses of animal matter.

In proceeding to a minute investigation of the chemical processes in the animal or vegetable organism, we usually begin by considering such questions as—whether the masses acted upon by different forces in vital phenomena differ essentially from those in which we have studied mechanical or physical forces?—whether all those differences which force themselves upon our notice in no small number and in a very decisive manner, on comparing together organic with inorganic, and organised with crystallised or amorphous bodies, are owing to essentially different causes, or arise simply from a multiplicity of intermerging forms, and only correspond to the more prominently marked points of limitation in the frequently intersecting series of qualities? This is not a question, however, which we purpose discussing at the present time; for, as we have already observed in our brief notice of it in the introduction to the theory of the Animal Substrata, it has been finally set at rest by pure chemistry. The belief which our predecessors cherished of an actual principle of vitality has passed away with them, and to attempt to attach even a semblance of reality to this exploded notion of a bygone period would be at once to condemn the most brilliant discoveries of the last few years, and indeed the whole labours of half a century, as the manifestations of mere delusive chimeras.

But whilst pure chemistry has shown us that the laws which control the cohesion of different atoms in stones and rocks are the same as those by which the persistence of the atomic composition of animal and vegetable substances is maintained, the theory of the animal substrata, juices, and tissues, affords a proof that the quality of the different particles of matter which serve as points of application for the active forces which exist in the animal body, invariably corresponds to the functions required for the performance of the purposes of life. When we pass in review the delicately linked series of chemical combinations taken by the animal body from that laboratory of all organic bodies—the vegetable kingdom—or generated anew within itself, the idea involuntarily presents itself to us, that the chemical quality of a substance for the most part corresponds to its physiological importance; thus we find that the more complex atoms, the chemical particles of which have a less stable equilibrium, occur especially wherever the higher functions of material life are manifested.

Thus, too, we had occasion to notice, at the close of our description of animal matters, that even those more organised atoms which constitute the more simple substrata of the animal tissues are always formed in accordance with the functions which they control or the forces with which they are connected. However strikingly this observation seems to be confirmed, wherever the chemical movements of the animal body fall under our notice, it need not excite our surprise; for when we only observe the known laws of molecular motions, we perceive that their manifestations in these particles of matter must be different from those in inorganic nature. The manifestation of each force is connected with the nature of the mass which is to be acted upon, whilst the effects depend upon the circumstances under which the force is brought to bear upon the mass. If, therefore, we wholly disregard the question whether other forces than those with which the physicist is familiar may not act upon these masses, such forces appertaining exclusively to life, it follows *a priori* that the resulting action of these physical forces will be very different when exercised upon inorganic particles, (which, although differently formed, present identical principles of structure,) than when applied to the simpler forms of mineral substances. This proposition requires no further demonstration, but it indicates the direction we must follow if we would attempt to trace the internal connection of vital phenomena in their individual phases, and thus investigate the various processes of animal life.

We have, in accordance with the plan of our work, passed in review the general mechanism of the animal organism, and considered the chemical nature of the individual parts; we proceeded next to investigate matter and its endless variety of forms, without however directing more than a cursory glance at the motions of the individual parts, or the various phenomena of physical life. We have now to enter into the phenomenology of the individual members of this vast series, postponing our investigation of the forces through the agency of which the phenomena are called forth, until we have gained a sufficient knowledge of the qualitative and quantitative relations of the individual phenomena. This is the simple and only practicable method of conducting every physical inquiry, and hence we ought not to neglect it in physiology. Nor can we enter into a causal investigation of the objects of our inquiry before we have considered the phenomena in the living organism from all points of view, and ascertained its relations of mass and weight. We shall have occasion to perceive, in our attempts to refer individual phenomena to their controlling causes, and to

ascertain the inner connection of their reciprocal effects, that a great number of vital phenomena stand in the simplest relations of dependence to well-known, so-called physical laws, or more general propositions; and that it is to the special mode of arrangement of the individual elements of motion, and to a complication of numerous conditions, that we must, at all events to a great extent, refer the specific character which is impressed upon vital phenomena. We certainly very often fail in solving the mystery of the internal association of phenomena, or the connection of the laws or forces by which they are controlled. Even in the case of a purely mechanical or purely chemical effect, we very frequently fail in comprehending the complication of circumstances which has given rise to the peculiar results manifested. We must not, however, regard the various interruptions which present themselves to our notice in the consideration of vital processes as a proof of the development of forces pertaining exclusively to life.

Molecular forces themselves, and the manifold complications which they undergo in accordance with different circumstances and relations of mass, are not yet sufficiently elucidated to enable us to trace the causal connection of all the phenomena to which they give rise even in the inorganic world.

How numerous are the actions of affinity which we have hitherto failed in referring to any general rules, or even to the leading principles of chemistry! We do not even know whether chemical combination is the sole effect of chemical affinity. But the simplest effects of cohesion and adhesion manifest themselves under such numerous and various circumstances, that physicists have been unable to elucidate the conditions on which they depend. Who would have believed some years ago that the most strongly developed chemical affinity might occasionally be destroyed by simple diffusion? or who would have ventured even a few months back to plunge his hands into molten glass, or to immerse a living child in melted copper? When experiments of this nature were attempted in former ages, mere vital force was regarded as too simple and inefficient to afford an explanation of this phenomenon; no power but the All-Highest being capable, according to the vulgar belief, of thus miraculously suspending the ordinary laws of life; yet this marvel, which still excites the wondering admiration of the ordinary spectator, admits of being reduced to very simple relations of cohesion. The effects of molecular forces have never been so thoroughly examined in all their bearings and modifications as to aid us in our consideration of the intricate mechanism of the innumerable results manifested in the animal

organism. Even now a Graham is devoting his energies to the elucidation of the numerous effects of diffusion, and we scarcely yet possess any solid basis for our views of the phenomena which are termed endosmotic. Yet, notwithstanding this great deficiency in our knowledge, the few certain conclusions which we have drawn from our experiments on diffusion and endosmosis have already largely augmented our knowledge of many of the processes in animal life. Our insight into the movements of matter is daily being enlarged by numerous contributions from able physicists, who have elucidated many points which had previously been enveloped in obscurity, and which, without such elucidation, might with equal propriety have been referred to either a vital or to any physical force. Such labours are daily supplying us with the compass and the quadrants by which we may safely steer our course across the vast sea of vital phenomena, and learn the position and reciprocal bearing of each individual point. It will be better, therefore, to wait patiently for the advent of the new discoveries promised to us by these researches, instead of selecting as our guide the mysterious vital force which does not even interpret to our own satisfaction the phenomena we desire to elucidate, but merely plunges us lower into those conflicting depths of physical inquiry in which so many bold adventurers have been already lost. In plain words, it would be far more conducive to the advancement of science, were we to direct our efforts to the task of referring vital phenomena to mechanical conditions, instead of resigning ourselves to the fiction of a general principle, which will never satisfy that natural striving of the human mind which seeks to embrace all phenomena in one ideal connection.

The living body itself is not the place where we should seek to investigate the forces by which the movements of animal matter are controlled, and it is only when examined externally to the organism that we can make them subservient to the elucidation of the phenomena of life. This is the course which has been pursued by physiologists of recent times, to whose researches we owe a very considerable number of the most interesting conclusions regarding molecular motions. When the scalpel of the anatomist has brought to view the delicate structure of all organic parts, and the mode of arrangement and the mutual relations of different phenomena have been studied, the physiologist endeavours to trace the causal connection of facts to definite laws, and seeks to refer the course of phenomena to other forces besides those which appertain exclusively to the internal mechanism of the body. Whilst in former times physical laws were often not

sufficiently taken into consideration in the explanation of vital phenomena, the tendency of latter times has rather been to attach undue importance to them. All things which did not admit of being referred in a simple manner to known mechanical means, were ascribed to vital force, which, although as yet unknown, might, perhaps, serve as a guiding light to future generations in their advance on the paths of physical inquiry. But it was forgotten that there are very many phenomena in inanimate nature which must be explained by physical laws, and that we have very slight knowledge of the laws of molecular motion. The many cases, too, have been overlooked in which chemical phenomena are opposed to all the ordinary laws of affinity, whilst the theoretical deficiencies of our highly vaunted science of chemistry have not been thoroughly admitted, notwithstanding the want of success which has attended all the attempts hitherto made to explain the highest chemical principles in simple mathematical symbols, and to calculate their results by simple formulæ.

When we consider the deficient state of our knowledge of many physical laws, and the varying circumstances by which their results are modified, we can hardly suppose that all the phenomena of animal matter can at present be referred to mechanical conditions, and we shall be compelled to admit that there are no grounds on which we can establish an exclusive vital principle by which the phenomena of life can be explained independently of purely physical forces. Physical inquiry demands that our investigations into the existence of a vital force should be preceded by a complete separation of all phenomena which can be referred to purely physical forces, from those which depend upon some force peculiar to life. Physical knowledge is, however, quite inadequate in its present state to afford proof of this nature, for which we must await a more perfect development of this branch of science. We are still ignorant of the relation borne by the obscure agency of the nerves to electricity; and, notwithstanding the attention that has been directed to the study of the phenomena of the nervous system, the physiologist would scarcely venture to determine whether these phenomena admit of being referred to certain physical relations, or whether we are compelled to assume the existence of some specific nervous agent peculiar to animal life. As, however, we are still unable to refer nervous actions and certain other phenomena of animal life to simple physical laws, we must leave the proof to those who, even in the present day, regard as undoubted the existence of a nervous agent or vital force. The correctness of the view which ascribes vital pheno-

mena to mechanical conditions, cannot be fairly tested till the existence of this new force has been proved; but how can such proof be adduced in reference to a force the simplest effects of which are unknown to us, and which differs from other forces merely by its disregard of all restrictions, and of the limits prescribed by physicists to laws? It may be briefly asserted that the exclusion of physical agency affords no proof of a purely vital force; and yet there is no other means by which its existence can be established. The physicist who rigidly follows the leading maxims of his own science, must admit the possibility of a vital force, although he may regard any proof of its existence as at present impossible.

The time has passed when the assumption of different vital forces was supposed to afford sufficient explanation of all or any alterations occurring in organised bodies, or when these same forces were fancifully represented as the architects of the organism, and the stewards of the vegetable and animal economy, providing all things, providently warding off all noxious matters, removing all that threatened evil, executing all useful things, and everywhere active, keeping a watchful guardianship over the whole organism. But physiologists still exist, who regard those phenomena in the vital economy, which we are as yet unable to explain on physical principles, as a proof of the existence of a specific vital force. Let us once more briefly consider the grounds which make such an assumption simply problematical.

If the proposition be established that no organised body can be formed from the fortuitous elements of inert matter, and if organised bodies must originate in organised structures only, and finally, if, without life, life could not be generated, the elaboration of organised bodies must depend upon that which is organised—upon life, or vital force. Such a sequence as this proves the impossibility of obtaining an insight, from a physical point of view, into the origin and development of organic matter. We must admit that in the physical sciences generally we meet with certain boundaries beyond which we are conscious that the human intellect never can or will pass. Thus astronomy, the most perfect of all the physical sciences, will never succeed in explaining how the planetary system, with its satellites, was first set in motion, or what gave the first impulse to the eccentric orbits of the comets which traverse our solar system. Notwithstanding Laplace's theory, we are ignorant of the primary cause of the formation of the earth; we are firmly convinced that, at a definite period of the earth's development, the seeds of all plants were

simultaneously scattered over its surface; we know that for thousands of years an exuberant vegetation covered our globe, before the sun had matured the first germ of animal life; and we are equally convinced that it was only subsequently to the most recent revolutions on the earth's surface that the higher animals were created, and that, last of all, Man appeared. But here the physical sciences lead us to a boundary, which we distinctly recognise as such, and know that we can never pass, without leaving the domain of physical inquiry for the regions of metaphysics. But it does not follow that because we are unable to recognise the origin of certain natural phenomena, we may not be capable of comprehending their subsequent course. The human mind does not turn aside from the study of the movements of the heavenly bodies, because it does not, and never can hope to know the origin of their motion; and its efforts have been successful in attaining the most exact acquaintance with the laws of those motions, and the course of the motion when once imparted, and has even been able to predict what those motions will be at a future period; for the laws remain everlastingly unchanged, although the *primum movens* cannot be recognised after it has once imparted the motion which obeys the laws. Thus, too, in respect to the primary formation of organised bodies, either as seeds or ova, no investigation will ever show how the germ originated, or what regulated the first creation of ova and seeds; yet, notwithstanding this, we are as well able to investigate the laws of the organic motion that has been induced, as to study the regular movements of the heavenly bodies in their orbits; for, as in the regions of space, the first moving force merely gave the impulse to motion and regularity, and did not again, by renewed influence, affect the motion imparted to the created body, so also when the force by which the germ was generated, had implanted in it the laws necessary to effect its development, and to control its further elaboration and assimilation, it ceased to interfere with the laws it had established; it gave to the living organism no guide or guardian by whose agency the sacred laws of its being were to be modified or miraculously suspended. The true miracle of nature is the unchangeable regularity of the course of all phenomena. Since, therefore, conformity to law has been implanted in organised bodies, we may hope, although perhaps at a later period, to examine the laws of organic nature as accurately as previous generations succeeded in elucidating the physical laws of cosmical phenomena.

Although in our study of the animal organism we frequently

meet with phenomena which we cannot deduce from known chemical principles, and which indeed seem to be in direct opposition to them, we must not at once conclude that the laws of affinity are partially or wholly inefficient in these cases; nor should we suppose that there is any marvellous intervention of some force acting with a definite purpose. The chemical force is not destroyed, but the external relations, which control its activity, are altered. Force is obviously nothing more than the expression of the cause of natural laws; if, therefore, facts do not accord with our laws, we must either have formed a misconception of the ideas of these laws, or, at all events, we must have imperfectly investigated the different circumstances under which they were exhibited. The result of forces (which, in a physical sense, is only a short expression for the laws) must necessarily be different under different conditions.

Albinus* took no superficial view of the organic activity in nature when he established the axiom that the essence of vital force consisted in motion. Even if this expression be far too general for organic action, it cannot be denied that we assume life to exist wherever we perceive a constant alternation of phenomena and incessant changes, induced by the constant motion of the molecules of the organised body, as well as of the organs themselves. Although Albinus overlooked the fact that, on the one hand, something more than this is necessary to vital action, (as we here for the most part consider the grounds and object of motion, often without comprehending its primary origin,) and that, on the other hand, we recognise a perpetual movement in the heavenly bodies without assuming that they are on that account possessed of life, this proposition is to a certain degree correct, when we limit it to the substrata of vital manifestations—to organic motion; for we find that wherever matter is endowed with life, its chemical molecules are endowed with incessant motion.

Metamorphoses are continually developed in the material substrata of the living body. Physical forces always strive to maintain themselves in equilibrium; the matter set in motion by them finds, or, at all events, may find, its centre of gravity—its point of rest. Physical forces continue to act upon matter after it has attained its position of equilibrium, for it is only by opposite actions that the equilibrium exists. A body which is moved by physical laws appears always to tend only towards a state of rest; inorganic chemistry continues active, and induces motion and metamorphosis until the closest affinities are satisfied.

* De naturâ hominis, p. 39.

The case is very different when physical forces act under organic conditions, or when motion occurs in organised bodies, for here we find a tendency to persistence; everything that is brought into the line of direction of these concurrent forces is impelled to similar motion, and although a temporarily preponderating force may be antagonised, equilibrium will not be induced; for equilibrium is rest, and in rest there is no life, and in equilibrium there is death.

If we may be permitted to bring prominently forward some few causes from the sum of the conditions under which physical forces act in the motion of living beings, there are three characteristic points which appear especially to challenge our attention. The question arises how this persistence of motion, which can only be maintained under purely mechanical conditions, can exist independently of vital stimuli. We are acquainted with a number of purely chemical motions or processes which require for their accomplishment a certain duration of time, or, in other words, a longer interval, to equalise all the conditions of affinity than is required for the usually instantaneous effects of chemical affinity. We need only refer to the solution of fibrin in nitre-water, to the decomposition of alcohol by caustic alkalies, to the formation of numerous compound ethers (Liebig*), and more especially to the processes of fermentation and putrefaction. In the meanwhile, notwithstanding the occasional constancy of all these chemical motions, they differ in a very marked manner from organico-chemical actions in living organisms. Thus in fermentation and putrefaction we observe that the chemical motion exhibits a tendency towards the simplification of the radical—a tendency to equilibrium; in these decompositions there are always produced more fixed combinations and more persistent bodies, until at length there are formed either undecomposeable radicals or their most constant combinations, upon which equilibrium or rest follows. We perceive no tendency of this kind towards equilibrium in chemico-vital motion; for here one motion is produced only in order to call forth some other motion, the object of the metamorphosis being merely to effect a new change. The molecular motion itself is thus maintained by motion, and gives occasion to new motion; a substance undergoing metamorphosis gives origin to a new substance, which in its turn becomes the source of new motion, that is to say, new substances are formed by chemical activity which are not characterised by their constancy, as in putrefaction and decay, but are distinguished by their marked

* Ann. d. Ch. u. Pharm. Bd. 65, S. 350.

tendency to generate new motion, new decomposition, and new metamorphosis. Hence we also observe that in processes of the highest vitality in the organs, the most decomposeable substances, even self-decomposing bodies, are formed. Diastase, ptyalin, and pepsin, the most readily decomposeable substances, are produced only during high organico-vital activity; but owing to the incessant metamorphoses which they undergo, even whilst they are being submitted to chemical investigation, they have been but imperfectly examined. It is not, therefore, the capacity for repose in inert matter, on which the persistence of motion, and consequently life, depends; for the return of the molecules to a state of rest is prevented in the same manner as falling when a man is walking or running. The chemical molecules are not in a condition of stable equilibrium or of the strongest affinity; but the act of falling, the more constant union, the suspension of motion, is prevented by another simultaneous motion, the centre of gravity becoming unstable, and the manifestations of affinity being kept *au courant*. In consequence of the variety of substances which are brought into contact with one another during the metamorphosis of matter in plants and animals, one molecular mass is hindered by another, during the general motion and transposition, from attaining its natural centre of gravity, and is constantly drawn aside into new directions at the time it was striving to acquire equilibrium by the most powerful forces of affinity. Many poisons destroy life merely by suspending the action of some of the factors of organic motion; in the same manner as in fermentation and putrefaction, the special exciters of these processes induce chemical equilibrium.

Organico-chemical motion is the most complicated of all molecular changes; for besides the many new substances formed at one spot and at one time from other substances, there also occurs in an equal degree a disturbance and a new arrangement of the particles of the previously formed bodies. We may here instance the muscular tissue, in which the muscular fibre is formed, and where, after it has continued for some time to subserve the higher purposes of life, it undergoes a new metamorphosis in the muscle, simultaneously with the formation of new fibre. Thus we have here, at one and the same spot, the beginning or origin of a substance, its persistence or adaptation, and its termination or dissolution. Occasionally, one or other of the factors of motion becomes consolidated, without passing through the general course of the ordinary phenomena; an aggregation of molecules is here brought to a state of chemical equilibrium, and forms a more constant combination; individual groups are brought into rest, and

become deposited; in this manner, for instance, fat and horn-cells are produced in the animal organism, and gum, resins, and oils in vegetable bodies.

If we consider life in the organic substrata from this point of view as an incessant movement of molecules and molecular aggregations, as an uninterrupted process in which beginning, progress, and termination of motions intersect one another at the same time, it will no longer excite our surprise that the chemist has hitherto been unable to trace physiologico-chemical processes in their various directions, to detect from amid a seeming chaos all the substrata which concur in effecting such a process, and to determine with exactness their different properties. Nor must the chemist flatter himself that he can at once, in the midst of the perpetual metamorphosis of matter, arrest the life and motion of the organic substrata, and thus examine the position of the chemical molecules at the moment of rest; and he would be equally in error were he to assume that the substances he has separated are entirely the same as they were when all the molecules in the organised body were in a state of vital motion. It is impossible to arrest at will the machinery of molecular motion, to bring the moved parts at once to rest and render them rigid, to make them maintain the same unstable equilibrium, or to separate the individual parts of this chemico-vital mechanism. As we are not able to analyse ferments because it is by the very act of self-metamorphosis that they generate fermentation, so also does it defy the efforts of the chemist to investigate organised matter itself; for his solvents and reagents affect only the products of molecular motion in the living body, but not the act of motion itself. If the scalpel of the anatomist, which only reveals to us the often-mangled structures of life, has yielded such grand and brilliant results regarding material life as to form the basis of physiology, what may we not look forward to from the attainment of a more profound insight into the molecular movements? or need we wholly despair of being able, by physical investigations, to discover some magnitudes which will enable us to calculate the highest unknown magnitude?

Many persons have found it very difficult to understand how inorganic matter derived from the external world, can become subject to organic laws within the sphere of the living organism, and undergo the metamorphoses appertaining to that sphere without the co-operation of dynamical laws belonging exclusively to life. It was thought that the magic circle of the vital principle was sufficiently restricted if the mineral substances which we meet

with in the organism were regarded as beyond the limits of vital force. Assimilation and reproduction, like growth, were regarded as inexplicable, according to physical laws. But although many individual points may defy all attempts at explanation, we cannot doubt that these phenomena must be susceptible of a general explanation; for if we limit ourselves to the known phenomena of motion, we shall find that there is not any indispensable necessity to assume that this kind of molecular motion requires the control of any such agent as vital force.

We meet with very many cases in which several bodies seem to induce in other bodies an action similar in force to the one they exhibit, although there is no appearance of a relation of affinity between the products of decomposition and those bodies which are still undecomposed. Organic chemistry is rich in cases of this kind, and similar instances are not wanting in inorganic chemistry; the most frequent and striking of these occur in the processes of fermentation; for we here find that a small quantity of a substance undergoing a definite metamorphosis, can induce a special form of decomposition or metamorphosis in an infinite quantity of some other substance. As the slightest contact with any individual point of matter in the molecules of iodide of mercury, arsenious acid, metallic iron, or fulminate of mercury, and in a hundred other similar substances, gives rise to an endless series of definite motions; so the smallest amount of a putrifying body is able to impart to the chemical molecules a definite motion, which is propagated in an uninterrupted sequence from atom to atom, and may thus call into existence new forms and new qualities. All these phenomena, which were formerly referred to a specific catalytic force, not amenable to any law, and which were first referred by Liebig to their true physical relations of causality, indicate the point of view from which we ought in a physical light to examine many of those vital phenomena which at an earlier period were ascribed solely to the *vis vitalis*.

The primary origin of all vital phenomena is as unfathomable a mystery as the first impulse by which suns with their planets and satellites were impelled in their orbits; but if we direct our attention to the motion once imparted to organic molecules, we shall be able to trace the co-operation of the laws of the impulse or propagation of motion in the development, growth, reproduction, and secretion observable in organised bodies. From our experience on these points we shall frequently see how it is possible that substances which appear in all chemical points to be opposed to one another, may present similarities. The germ in the egg and in the

seed is surrounded by substances whose molecular arrangement may be disturbed by a slight impulse, and made to undergo metamorphosis. By a slight transposition of its atoms, or by the elimination or absorption of water, the starch of the cotyledons is very readily converted into bodies bearing very little resemblance to itself, but most extensively diffused through the vegetable kingdom, as, for instance, into gum, mucilaginous matter, cane and grape sugar, cellulose, &c. The white of egg is in like manner capable of undergoing the most various alterations without losing the most essential atoms of its constituents; albumen, the first and most important of animal substances, is a perfect *Proteus* in its metamorphoses, assuming the most singular forms both in animal and vegetable bodies; yet we everywhere meet with the same groups of atoms, although the molecular arrangement is constantly changing in order to invest them with different physical and even chemical qualities; and thus chemistry has hitherto failed in tracing the molecular motions of albumen in all its forms. Nature has surrounded the germ with variable substances such as these, whose molecular structure has so unstable a centre of gravity that whenever the slightest motion occurs in it, it readily extends to the other molecular masses; nature has, therefore, surrounded the mysterious source of life with substances which readily admit of being drawn into its current. Are we to believe that vital force resides in the germinating seed for the purpose of fabricating sugar from starch? or that the impulse of chemico-vital motion is propagated to the oscillating molecules, because we can communicate such an impulse to starch within a digesting flask as to change the grouping of the molecules, and alter the direction of their centre of gravity? The latter view, at any rate, furnishes some explanation of these processes, and is supported by numerous analogies, whilst the former is a mere ideal mystification of a simple fact obvious to the unaided senses. It would appear as if all the starch and all the albumen were drawn into the movement of germ-life before the stream of life had acquired sufficient force to increase its own mass by incorporating other molecular parts having a more stable centre of gravity. It is now only that the quantity of chemico-vital motion seems sufficiently great to impart to bodies having a more stable equilibrium a motion which is then regulated by physical and vital laws. The accession of new matter to the moved mass does not diminish the velocity of vital motion; the whole quantity of the motion is increased; for the destruction of the chemical masses which previously rested upon a solid basis gives occasion to a new impulse and to

renewed motion; as, for instance, a single atom of oxalic acid is able to convert a hundred and more atoms of oxamide into oxalate of ammonia, or as a single vesicle of air can produce fermentation in infinite quantities of vegetable juice, or as the avalanche which increases in mass as well as in velocity as it rushes down the snow-covered declivity of the mountain side. This kind of vital motion is at least not at variance with physical laws, whilst it presents analogies with purely mechanical motions. It is these analogies which the investigator of nature must endeavour to detect in vital motion, in order to deduce from the known factors the still unknown coefficients of this motion. The vital law cannot be discovered and elucidated until the chemical and physical laws by which these motions are regulated have been thoroughly investigated and distinctly recognised.

It appears strange, and scarcely reconcilable with physical laws, that the molecular motions in the living organism should so rarely deviate from their prescribed course, notwithstanding the innumerable causes which are constantly threatening to disturb them. Organic vital motion is neither straight nor uniform; all its manifestations exhibit an oscillating character, appearing invariably to incline first in one and then in another direction, although some compensating property seems to prevent excess beyond a certain limit. As the influence of heat is compensated in the animal body by the increased evaporation of the fluids, like the action of the same agent on the compensation-pendulum; so also in organic motion, notwithstanding its extreme fluctuations, regularity is maintained by some one predominant force being spontaneously arrested, and by the simultaneous action of different particles in motion, which neutralise on the one side what might from the other side give rise to a disturbance in the regularity of the organic motion. The existence of this compensating capacity in organic motion meets with the fullest confirmation in its abnormal or pathological phenomena, which have consequently been regarded as affording the most convincing proofs of the reality of a wise and provident vital principle.

Although the dogma of the vital force cannot be wholly passed by in a text-book of physiological chemistry, we should not have treated it with the completeness with which we formerly* considered it, if there were not some cause of apprehension that there might occur a reaction in reference to this question, and that vital force, even if it did not regain its former position, might yet obtain

* In the first part of the original edition.

a recognition injurious to scientific inquiry. The imperfect experiments which have been made with a view of deducing certain phenomena in the living organism from some simple physical law, or bringing them into harmony with some ordinary experimental fact, although these phenomena probably depend upon a sum of many individual forces acting under the most various modifications, simply afford evidence of the superficial and deficient physical and chemical attainments of those who instituted them, and have probably done more to support the belief in a vital force, than the fact that we have as yet no prospect of being able to refer the formation of cells and tissues, and the suitable conformation of all the individual parts of the animal organism to definite physical and chemical laws.

Origin of Organic Matter in the Vegetable Kingdom.

Before we proceed with our general review of zoo-chemical processes, we must consider the locality and the relations under which organic matter is mainly formed. Theoretical chemistry shows us that the composition and all the properties of those substances which are especially named organic, are not only not opposed, but actually afford the most brilliant confirmation of all the more general laws which refer to this department of chemistry. There seems, therefore, considerable probability that the formation of organic matter from inorganic substances may be due to the action of the more general laws of physics and chemistry. If affinity, like gravitation, be an integral property of matter, the first indications of the formation of organic matter must necessarily furnish the best point from which to investigate the chemical laws which control the generation of organic from inorganic substances. The relations on which such formations depend have not, however, been examined with sufficient exactness to admit of our representing the formation of organic matter by simple formulæ, based upon direct observations. Whilst an opinion prevailed in earlier times that plants, like animals, required for their well-being to appropriate to themselves at least some definite, but not inconsiderable, amount of organic matter in the form of humus, Ingenhouss held the opinion that plants derive their nutriment solely from inorganic nature; and this view has been most ably defended by Liebig, who has shown that the

vegetable kingdom collectively, or at any rate the great majority of vegetable substances, is nourished solely by carbonic acid, water, and ammonia, and that, consequently, all organic bodies in the vegetable kingdom are generated solely from these three inorganic substances.

Priestley and Sennebier first made the observation that the leaves of plants, when exposed to solar light, *absorb carbonic acid and in its place exhale oxygen.* The admirable experiments of Saussure, and the later researches of Grischow, Boussingault, and others, have elucidated many points connected with this subject. We now know that it is not only direct solar light, but also ordinary refracted light, that produces this phenomena, which depends not upon the heating or the chemical rays of the spectrum, but mainly upon its yellow and green rays (Draper), and that, moreover, the green parts of the plant alone possess the faculty of exhaling oxygen after absorbing carbonic acid. Plants only exhale oxygen after the absorption of carbonic acid, which is probably taken up through the roots from water or through the leaves from the air. Boussingault has especially drawn attention to the extraordinary rapidity with which the leaves abstract carbonic acid from the air. The quantity of oxygen that is exhaled corresponds very nearly with the amount of carbonic acid which has been absorbed. These experiments were not, however, conducted with the exactness necessary to warrant us in drawing definite conclusions; for while the volume of exhaled air was perfectly equal to that of the absorbed air, there was always found in the exhaled air a small quantity of nitrogen, the source of which could not be clearly ascertained. The experiments appear, at all events, to prove that there is always rather less oxygen developed than is contained in the carbonic acid, and consequently, that the entire volume of the oxygen is not returned to the air from the carbonic acid. Although a portion of this gas may pass into those organs of plants which absorb oxygen, although they are not green, certain chemical and other grounds render it more probable that a large amount of the exhaled oxygen may be derived from water, and that the carbonic acid cannot therefore be decomposed at once into carbon and oxygen. It would also appear, from the experiments of Saussure and others, that the amount of exhaled oxygen does not depend upon the mass so much as upon the extent of surface of the green parts of plants.

The undoubted fact that plants reverse this process during the night, by developing carbonic acid after they have absorbed oxygen,

as is done during the day by those parts of a plants which are not green, led many physiologists to doubt whether the principal source of the carbon in plants was derived from the deoxidation of carbonic acid, which takes place in solar light; whilst, moreover, Saussure's experiments seemed to prove that at least one-twentieth of the carbon absorbed by the plants during this process could not be derived from the carbonic acid. It was believed that there must be some truth in the popular notion that the humus, that is to say, the decaying remains of vegetable and animal matter, serves the living plant as a highly carbonaceous nutrient substance, at least in respect to this one-twentieth. Although it cannot be denied that a certain number of plants, amongst which we may reckon many of the parasitical plants, and all plants which are not green, cannot draw all their carbon from the carbonic acid of the air and water, this no more proves the incorrectness of Liebig's view than the fact that oxygen is exhaled in solar light by certain green infusoria, as *Euglena* (which, moreover, contain a starch-like substance) refutes the view that the vital process in animals is constantly combined with an absorption of oxygen and an exhalation of carbonic acid. Although many plants may thrive better in a soil rich in humus than in one in which they merely obtain the necessary mineral nutriment, this beneficial effect may be owing to many other conditions besides the amount of carbon contained in the soil; for as the humus consists of substances undergoing decomposition, it must of itself supply an abundant source for the formation of carbonic acid.

Liebig refers this nocturnal development of carbonic acid to a purely mechanical cause. It is well known that plants absorb indiscriminately all substances held in solution in water, but that they give off, either by their roots or through other parts, all matters which may injure their vital activity; and that all terrestrial as well as atmospheric water contains larger or smaller quantities of carbonic acid, which, according to Liebig,* is not assimilated during the night, but is again evaporated in an unchanged condition through the leaves with the water. But whilst Liebig regards the development of carbonic acid as purely mechanical, he considers the nocturnal absorption of oxygen to be a purely chemical process, and shows that the variations in the quantity of

* Die Chemie in ihrer Anwendung auf Agricultur u. Physiologie, 6 Aufl. 1846, S. 3-253 [or English translation, London, 1840, pp. 1-215]; Chemische Briefe, 1851, S. 240 ff. u. 629 ff. [or Letters on Chemistry, 3rd edition, 1851, pp. 176 and 506].

the oxygen that is absorbed are entirely dependent on the chemical constituents of the leaves. Thus, for instance, leaves which are proportionally rich in substances poor in oxygen, as for example, resinous ethereal oils, which even in their isolated state readily become more highly oxidised when exposed to the action of the air, are also found to absorb a relatively larger quantity of oxygen in the dark.

A complete process of acidification during the night, as the effect of oxidation, is occasionally met with in the leaves of certain plants, as, for instance, the *Cacalia ficoïdes*, *Cotyledon calycina*, and others, which, after being tasteless at noon, have a bitter taste in the evening, but are sharply acid in the morning.

Pelouze has shown that tannic acid is converted into gallic and carbonic acids by the absorption of 8 atoms of oxygen ($C_{18} H_8 O_{12} + 8 O = 4 CO_2 + 2 C_7 H_3 O_5 . HO$). We cannot wonder at the fact observed by Saussure, that the leaves of the oak, which are so rich in tannic acid, should absorb 14 times their volume of oxygen during 24 hours when in the dark, whilst the tasteless and scentless leaves of the *Agave americana* can scarcely absorb 3-10ths of their volume in the same time. The leaves of the white poplar, which contain a very resinous or oxidisable oil, absorb as much as 21 times their volume of oxygen in 24 hours.

Without entering more fully into the question of the respective results of these two reciprocally suspended processes of the vegetable kingdom, we would simply observe that, notwithstanding the grounds on which Liebig supports his view of the purely chemical nature of the absorption of oxygen, this process and the separation of carbonic acid, appear, from numerous phyto-physiological experiments, to stand in a more direct relation to the whole life of the plant; and that, in the vegetable kingdom, processes of oxidation also occur in addition to the preponderating processes of deoxidation, in the same manner as we find that, in the animal organism, where life is so thoroughly characterised by continuous oxidation, processes of deoxidation may yet also occur, as, for instance, in the formation of fat from sugar and amylaceous substances. This is, however, so decidedly a purely phyto-physiological question, that it scarcely falls within the scope of our inquiries. According to our view, Liebig has given the most striking and ingenious proofs that the vegetable kingdom derives its large supply of carbon from the atmosphere alone, and that plants alone possess the faculty of generating organic matter from inorganic substances.

When we consider that the atmospheric air contains only 1-1000th of its volume of carbonic acid, it might at first sight appear as if the atmosphere could not supply plants with all their carbon—an opinion which was once generally entertained; but certain simple calculations made by Liebig show that, instead of believing the carbonic acid in the atmosphere to be insufficient for the growth of plants, we might rather wonder how it is that, notwithstanding the vegetable kingdom, the quantity of carbonic acid in the atmosphere has not been considerably augmented in the course of ages. The atmosphere exerts a pressure of 2216·16 lbs. on every square foot, and if it were as thick in all parts as it is at the surface of the sea, it would extend 24,555 Paris feet in height, or, after excluding the aqueous vapour, 22,843 feet, or 1 German geographical mile [about 8,100 yards]. If the radius of the earth be assumed at 860 such German miles, the volume of the atmosphere (at the pressure of an atmosphere of mean temperature) must be equal to 9,307,500 such cubic miles, in which, in addition to 1,954,578 cubic miles of oxygen, there would be about 3,862·7 cubic miles, or about 28 billions of cwts. of carbonic acid—a quantity which must be more than sufficient for the wants of all the vegetables occurring on the land or in the water of our planet.

If, on the other hand, we consider that enormous masses of carbonic acid are continually being conveyed to the atmosphere from the earth's surface, we cannot help wondering that it should have experienced no sensible increase in the amount of the carbonic acid which it contains; at all events, there has been no change in it during the period that has elapsed since the destruction of Pompeii, in the year 79 A.D. (as is proved by the analyses of air which had been contained in funeral urns which had been excavated from that city); whilst, on the other hand, geological investigations have rendered it almost certain that at some definite period, ages since, and long before the higher forms of animal life had appeared upon the earth, the atmosphere was far richer in carbonic acid than it is now. A rough estimate of these relations yields the same numbers which Liebig has deduced from a more complicated calculation. Thus, for instance, if a man daily consume 45,000 cubic inches of oxygen, which would give 9505·2 cubic feet for the year, 9 billions and 505,200 cubic feet of oxygen will be abstracted from the atmosphere by a thousand millions of men; and if, further, it be assumed that about double this amount of oxygen is lost by the respiration of animals, and by the processes of decomposition and combustion, it follows that

all the oxygen of the atmosphere would be exhausted in 800,000 years. This constancy in the quantities of oxygen and carbonic acid during 1800 years would therefore be wholly inexplicable, if we did not perceive that the growth of plants furnishes the means of abstracting from the atmosphere the carbonic acid which has been conveyed to it, whilst the discovery of inexhaustible deposites of carbonaceous vegetable *débris* furnishes one of the most striking explanations of the diminution of carbonic acid since the pre-adamite age.

When plants are introduced into an atmosphere containing no oxygen, and care is taken that the oxygen which they exhale by daylight is absorbed by iron filings or other means, they wither as rapidly as they would in an atmosphere devoid of carbonic acid, or in the dark, where they could not decompose the carbonic acid. These and similar experiments certainly indicate that the oxygen stands in a definite relation to the whole life of the plant; and, on this account, many of the most distinguished physiological botanists have held the view that oxygen gas is a true vital air to plants as well as to animals, with this difference only, that plants possess at the same time the power of generating for themselves the oxygen they require (H. Mohl).*

Liebig has shown that the humus of the fertile soil is not one of the humus acids of chemists, and that it cannot serve directly for the nourishment of plants, but that as it is formed by the decomposition of organic substances, it is only by means of the products of its decomposition, and by the carbonic acid which is formed from it, that it can supply plants with nourishment; while, on the other hand, the manure promotes the growth and thriving of plants less by the quantity of nitrogen and carbon which it contains, than by the large amount of mineral substances, which are equally important to the development of plants as water and carbonic acid.

We very rarely meet with fossil roots, and the plants belonging to an earlier world usually appertain to genera which are distinguished by the smallness of their roots; the first plants whose seeds were scattered over the surface of the earth found no humus from which they could extract nourishment, but shot luxuriantly forth beneath a dense atmosphere, abundantly charged with carbonic acid, which yielded them copious supplies of carbon, although the sun's light, which was variously refracted through the denser

* Handwörterb. d. Physiologie. Bd. 4, S. 235-250 [or Henfrey's Translation of Mohl, On the Vegetable Cell. London, 1852, pp. 77-93].

strata of air did not fall directly upon them. Thus we find even now that the luxuriant plants of tropical climates have very small roots; consequently such plants can scarcely receive the adequate amount of nourishment from this part of the vegetable organism.

Everywhere on the earth's surface we find that the increase of the humus depends upon vegetation. Plants spring forth on the naked rock, which must derive their nourishment solely from the atmosphere, and afterwards dying and mouldering away, they serve as a support for other plants; if, however, these plants absorbed for their nourishment the carbon contained in the mouldering vegetable *débris*, vegetation would soon cease, and the naked rock would be again exposed to view. In the virgin forest the remains of numerous generations of plants are accumulated upon one another; each layer of plants serving in its turn to increase these vast accumulated strata of humus. A large quantity of carbon is generally abstracted year by year from cultivated woods and fields, yet this does not prevent grasses and trees from springing up unchanged, and attaining their full growth without manure or any adventitious supplies of humus. How small a quantity of carbon is added to a cultivated farm by the annual amount of manure used on the land, and yet what immense masses of this substance are extracted each year in the form of fruits and straw, which are only again returned to the earth in the form of carbonic acid by the respiration of animals, and by the processes of combustion and decomposition!

It cannot be denied that small quantities of humus-like substances may pass into plants, in as far as the roots indiscriminately absorb the substances presented to them; but even if the above remarks show that the quantity thus taken up must not be regarded as inappreciably small, the fact that the humus acids form with bases insoluble salts, which consequently can scarcely enter into vegetable bodies, proves further that very little importance can be attached to this circumstance. Moreover, humus which is exposed to the natural action of the weather gives off a very small quantity of matter soluble either in water or lime-water.

The composition of most vegetable substances shows that *water* must undergo decomposition in plants during the production of organic matter; for, although we meet with certain substances in the vegetable kingdom in which oxygen and hydrogen occur under the same relations as they occur in water, we find many others in which the amount of oxygen falls far below that

of hydrogen, as, for instance, the resins and fatty oils; and there occur some combinations of carburetted hydrogen which are entirely free from oxygen, as, for instance, the ethereal oils and caoutchouc. A decomposition of water may also be more readily explained from a chemical point of view, than a reduction of the carbonic acid; Alexander v. Humboldt has even observed a development of hydrogen during the vegetation of several fungi.

We possess very few reliable experiments from which we can ascertain the relations under which plants generate organic matter from water and carbonic acid during their exposure to the action of the sun's light. According to certain observations of Saussure, a plant of *Vinca minor* generated, under definite conditions, a quantity of organic matter, in which there were contained 40·87% of carbon. In two plants of *Mentha aquatica* there was organic matter produced which contained 50% of carbon.

The *origin of the nitrogen* in plants is a subject of far more difficulty; for whilst carbonic acid and water are conveyed to plants from almost every direction and under all conditions, we are unable to detect the source from whence plants derive their nitrogen. Both Saussure and Boussingault* have shown by the most exact and ingenious experiments, that plants are unable to condense free nitrogen from the atmosphere, and to elaborate it into organic matter; and they regard it as probable that nitrogen passes into plants only in the form of soluble nitrogenous products of decomposition of organic matter, and more especially in the form of ammonia. Here again it is to Liebig that we are indebted for the discovery of the hidden sources of this important element of vegetable nutrition. Liebig has shown that the origin of the nitrogen must be referred to the direct contact of ammoniacal salts with plants, seeing that he found considerable quantities of these salts in many vegetable juices. The juice of the maple, the red beet, the birch, fresh tobacco-leaves, the tears of vines, and all blossoms and fruits, contained a certain amount of ammonia, without there being any indication that decomposition had set in. Exact calculations show that far more nitrogen is abstracted from well-cultivated fields than could have been conveyed to them by manure, or any other means. It has been seen from experiments on the solid excrements of animals, that ordinary solid animal dung, so far from containing much nitrogen, often contains mere traces of it, and that such manure is entirely inadequate to yield to plants the amount of nitrogen which is

* Ann. de Chim. et de Phys. T. 67, p. 5, et T. 69, p. 353.

found in them. Whence, then, do forest trees derive their nitrogen, as they can never have been manured with animal dung?

Until Liebig demonstrated the fact, it was not known that a constant quantity of ammonia was always present in the atmosphere, and that rain and snow contained determinable quantities of salts of ammonia. There can be no doubt, however, that nitrogen is supplied to plants as food in the form of salts of ammonia; but, on the other hand, Liebig's view, that the atmosphere is the sole source from whence plants extract their salts of ammonia, has met with considerable opposition. Boussingault and Liebig have endeavoured to prove from a calculation of the quantities of ammonia present in rain-water, and of the annual amount of rain, that the ammonia extracted from the atmosphere by plants is quite sufficient to form those nitrogenous compounds which we discover in the products of our annual harvests; and they have also drawn attention to the fact, that there are present in the humus, in dung—in short, in every fruitful soil—substances, which have the power not only of fixing the ammonia of the water, but also of absorbing ammoniacal vapour directly from the atmosphere. Bouchardat's observation, that salts of ammonia exert a poisonous action upon plants, even when diluted 1000 or 1500 times, may perhaps depend upon their unsuitable form, and probably upon their insufficient degree of dilution; but it in no way refutes the general hypothesis that plants derive their nitrogen from ammonia; perhaps Mulder's* conjecture may also be correct, that the ammonia passes into plants in combination with organic acids, and that in this form it exerts no deleterious action on these organisms. It would appear from most of the experiments which have been made in reference to the absorption of ammonia by plants, that the roots are designed for the assimilation of salts of ammonia to the same extent at least as the green parts serve for the absorption of carbonic acid.

In the putrefaction of nitrogenous substances, there is a development of carbonate of ammonia from the beginning to the end of the process; its great volatility causes it speedily to be given off to the atmosphere, from whence it is again precipitated with the water in the form of rain and snow, and is thus returned to the vegetable kingdom. If we assume that every pound of rain-water contains only half a grain of ammonia, there must be a sufficient quantity of this substance in the atmosphere to supply

* Versuch einer physiol. Chem. S. 715-752 [or English translation, pp. 651-691].

all the plants existing on the earth's surface with the nitrogen requisite for their growth and perfect development. Ammonia has also been found in every kind of water occurring on the surface of the soil, in sea-water as well as in running springs, and has been extracted from the greatest depths of the earth; as, for instance, with boracic acid from Castel Nuovo, Cherchiago, and other volcanic districts.

Animals, when they have ceased growing, restore to the outer world nearly all the nitrogen which they take up with nitrogenous substances, and the very exact determinations of Boussingault and several other inquirers show that the quantity of nitrogen given off from the animal organism after the termination of growth equals that which is introduced, and that the amount of nitrogen present in full-grown animals varies only very slightly. Ammoniacal gas is given off directly during respiration; nitrogenous matters are also far more abundant in the fluid than the solid excrements, and they very readily become decomposed into ammoniacal combinations.

The reason of the beneficial effects of gypsum and of burnt clay as a manure has not hitherto been very clearly explained; but Liebig is certainly quite correct in referring it to the property possessed by these substances of fixing ammonia. The gypsum undergoes decomposition with the carbonate of ammonia in the atmosphere, forming sulphate of ammonia, which does not evaporate with the same rapidity as the carbonate. It has been long known that alumina and oxide of iron possess the property of absorbing ammonia. This same property of absorbing ammonia is observed in the case of powdered charcoal and decaying wood, the former of which condenses 90 volumes, and the latter 72 volumes of this substance. Mulder includes amongst the substances which fix the ammonia in a rich soil, the five acids which he discovered in the humus, namely, ulmic, humic, geic, crenic, and apocrenic acids. These acids, which are formed during the decay of animal as well as vegetable substances, decompose, according to Mulder's view, the carbonate of ammonia which is conveyed to the soil by rain, and, having thus become soluble, are transferred, in the form of ammoniacal salts, to the roots of plants, where they are very rapidly decomposed (even in the extreme ends of the root-fibrils), and are converted into other bodies.

Fresenius* found, on an average, 0·133 parts of ammonia in a million parts (by weight) of air. Now, if we adopt Marchand's

* Ann. d. Ch. u. Pharm. Bd. 64, S. 101-106.

estimate of 5,263,623,000,000,000,000 kilogrammes as the weight of the atmosphere, and if it contained in all regions equal quantities of ammonia, the amount of the latter would be 2,646,404 kilogrammes. Horsford* found a much larger amount of ammonia than this in the atmospheric air; the greatest quantity was observed in July, when there were 47·63 parts in one million parts (by weight) of air; the smallest quantity noted was in December, when there were only 1·2171 parts. It would appear from the observations of Horsford, that the quantity of ammonia in the atmosphere is at its maximum in the summer months, when the sources of ammonia are most abundant, and when it is not so frequently carried off by rain and snow as in winter, and it would seem to diminish in an almost constant ratio towards the winter.

Liebig calculates that if 1 lb. of rain water contain only half a grain of ammonia, an area of 2,500 square metres will receive in the course of the year with the rain (which amounts to 2,500,000 lbs.) nearly 80 lbs. of ammonia, or 65 lbs. of pure nitrogen. This would be far more than is contained in the form of glutin and albumen in 2,650 lbs. of wood, or 2,800 lbs. of hay, or 200 cwt. of beet-root (this being the respective produce of an acre of wood, of meadow, and cultivated land).

Several nitrogenous substances which we constantly meet with in almost all plants, and more especially in their seeds, contain a certain amount of *sulphur*, and in addition to these there are the highly sulphurous ethereal oils, which may be extracted by distillation with water from several species of the Crucifers. As the air, rain, and ordinary spring-water, contain nothing beyond the merest traces of sulphuretted hydrogen, plants must obtain the necessary amount of sulphur from contact with alkaline sulphates, and especially the sulphate of ammonia. The sulphuric acid is then probably reduced by the same processes by which the deoxidation of the carbonic acid is effected. It is therefore obvious that the roots of plants are the organs through which sulphur is absorbed.

Having briefly considered the nature of vegetable nutrient matters, and traced their various sources in inorganic nature, we have next to direct our attention to the mode in which this inorganic material is elaborated into organic matter in plants. We should, however, most assuredly arrive at very incorrect conclusions, were we to attempt to explain the formation of organic matter in plants without at the same time taking into considera-

* Ann. d. Ch. u. Pharm. Bd. 74, p. 243.

tion their mineral constituents. When we reflect that no plant can exist independently of certain *mineral constituents*, and that these occur only in certain definite quantities, and that some bases only, such as soda or potash, lime or magnesia, occur in plants,—and when, finally, we observe that these mineral substances are accumulated in very different proportions in the various organs of plants, and in accordance with the different periods of their development, although they present tolerably uniform relations under similar conditions and in identical organs,—we are necessarily led to the idea that these substances exert a definite influence upon the life of the whole plant, and upon the origin of its organic constituents from carbonic acid, water, and ammonia.

The bases we have enumerated are generally found in the ash combined with carbonic acid, although in the living plant they more commonly occur in combination with organic acids, as neutral or acid salts. Liebig, in his notice of these substances, has drawn attention to two much-disputed points of discussion: whether one base may be replaced by another in a plant, and whether the sum of the oxygen contained in the base is always one and the same for each species of plants. Although we must for the present regard these propositions as questions which still require a more special solution, it must be admitted that within certain limits they would appear to derive confirmation from several established facts; for although we find in the older experiments of Saussure, as well as in the more recent numerous analyses of vegetable ashes instituted by Emil Wolff,* by Wiegmann and Polstorf,† and by Staffel,‡ many facts which seem to be opposed to these general propositions, it must be remembered that even in vegetative life a number of relations present themselves to our notice, whose actions on these more general laws cannot be wholly overlooked. It may perhaps be maintained that these hypotheses of Liebig's have not been proved with sufficient precision; but, on the other hand, the few points in which they admit of dispute are not of sufficient importance to warrant us in regarding them as wholly controverted. We have still so imperfect a knowledge of the relations existing in the nutritive process of vegetable organisms, that it is much less easy to establish a convincing refutation than to adduce a strict proof.

In addition to alkaline carbonates, we likewise find alkaline

* Journ. f. pr. Ch. Bd. 44, S. 385-488, u. Bd. 52, S. 37-122.

† Ueber die anorg. Bestandtheile d. Pflanzen. Braunschweig, 1842.

‡ Archiv. d. Pharm. 2 R. Bd. 64, S. 26-47.

sulphates, and especially alkaline phosphates, in the ashes of plants. These are not uniformly distributed throughout the entire plant, but are chiefly accumulated, as E. Wolff's experiments have shown, in the leaves, and still more abundantly in the seeds. As the careful observations made in relation to their occurrence appear to prove that a plant can scarcely thrive without these salts,—for although it may bear scanty blossoms, it never arrives at fructification,—it can scarcely be doubted that they constitute an essential requirement of vegetable life and are true elements of nutrition.

We will here briefly notice some few facts which may serve as illustrations of the above remarks. Liebig was principally led to the establishment of these hypotheses by the following analyses of the ash of fir and pine-wood taken from trees which grew in various localities. Saussure found 1·187% of ash in the wood of pine-trees growing on Mont Breve, and 1·128% in the same kind of wood from Mont La Salle. The following is the analysis of 100 parts of the ash of the pine-wood of Mont Breve:—

Carbonate of potash	.... 3·60 ;	in the potash there were	0·415	of oxygen.
" lime	.... 46·34 ;	" lime "	7·327	"
" magnesia	.... 6·77 ;	" magnesia "	1·265	"
Sum of the carbonates....	56·71 ;	Sum of the oxygen....	9·007	

A hundred parts of the ash of the pine-wood from Mont La Salle yielded no magnesia, but gave the following result:—

Carbonate of potash	.... 7·36 ;	in the potash there were	0·85	of oxygen.
" lime	.... 51·19 ;	" lime "	8·10	"
Sum of the carbonates....	56·55 ;	Sum of the oxygen....	8·95	

This relation is still more strongly manifested in two analyses of pine-ash made on French (Allevard) and Norway pine by Berthier, for here the difference between the soluble and insoluble salts in the two ashes is much more considerable than commonly occurs. In the ash of the French wood, Berthier found:—

Potash and soda	.... 16·8 ;	in which there were	3·57	parts of oxygen.
" lime	.... 29·6 ;	"	8·36	"
" magnesia	.... 3·3 ;	"	1·26	"
Sum of the bases	.... 49·7 ;	Sum of the oxygen	13·19	

The same observer found the following results in his examination of Norwegian pine:—

Potash	.... 14·1 ;	in which there were	2·4	parts oxygen.
Soda	.... 20·7 ;	„	5·3	„
Lime	.... 13·6 ;	„	3·82	„
Magnesia....	.... 43·5 ;	„	1·69	„
Sum of the bases	52·75 ;	Sum of the oxygen	13·21	

We must abstract from the oxygen of the bases in the first analysis 0·53 parts, and from that of the second analysis 0·79 parts, which belong to the bases which are combined with sulphuric and phosphoric acids ; so that there would be 12·66 parts of oxygen for the first, and 12·42 for the second determination of oxygen.

The idea that these equal quantities of oxygen indicate that there are equal quantities of acid to be saturated in the fresh plant, seems so obvious that its correctness might have been *à priori* suspected. At the same time, it was to be expected that this proposition would, under varying circumstances, be open to nnmerous exceptions, and that the direct results of the ash-analyses would rarely so accurately coincide as in the instances we have recorded. It is not, however, solely on account of their basic character that these alkalies and earths are necessary for certain plants ; for we know, for instance, that in very many plants the potash at all events cannot be thoroughly replaced by soda ; thus, for example, scarcely a trace of soda can be found in the ash of the horse-chesnut, even when the tree has grown in a soil in which this alkali abounds (E. Wolff, Staffel). The salts of soda are indeed absorbed in such cases, like other substances which are unsuited to the nutriment of the plant, but they are then speedily excreted, and principally by the roots.

We find in the ash of many plants, amongst others in that of the Cacti, that there is a much larger amount of carbonate of lime, and therefore a higher number for the oxygen of the bases, than corresponds to the true nutrient process of the plants. The carbonate of lime is here in part produced from the oxalate of lime, which is frequently deposited in the cells in a crystalline form, either as dead matter or as an excretion. Carbonate of lime is also deposited in a similar manner in many plants.

An exception to this rule, which may, however, be regarded as a proof of the correctness of the main proposition, is furnished by Liebig's discovery of the frequent occurrence of vegetable bases under relations in which the plant could not be supplied with any abundant amount of mineral constituents. Liebig draws attention to the fact that the quantities of the alkaloids found in cinchona

bark, opium, and the potato plant, are always large in an inverse ratio to the small amount of mineral bases which they contain.

However restricted may be the sense in which we interpret many of Liebig's propositions, it is most clearly apparent, from all exact examinations of vegetable ashes, as well as from the careful observations of the influence of individual salts as manures, that the alkaline carbonates and their phosphates are of the highest importance in the different processes in the life of plants. It would carry us too far from the scope of our inquiries, were we to enumerate all the facts relating to this subject, with which we have been long acquainted; and we will therefore content ourselves with referring to some few of the results which have been obtained from E. Wolff's admirable investigation of the mineral constituents of the horse-chesnut. The carbonate of lime predominates in the bark and in the wood, whilst the fruit and leaves contain far more carbonate of potash than the bark and wood. Phosphoric acid is most abundant in the flower-stalks and kernels, whilst sulphuric acid and silica predominate in the leaves. In the horse-chesnut, very simple ratios exist between the quantities of oxygen in the bases combined with carbonic acid in the different parts of the plant (the carbonates being calculated for 100). The quantity of oxygen in 100 parts of the alkaline carbonate from the ash of the bark amounted to 27, that from the wood and leaves to 24, that from the leaf-stalks and brown husks of the ripe fruits to 21, and that from all the other parts of the plant which were examined to 18, which corresponds with the simple arithmetical progression of 9:8:7:6. Wolff found that the ratio between the soluble and the insoluble constituents was very simple in all parts; thus, for instance, it was as 4:6 in the fluid circulating between the wood and the bark, and the same in the leaves, while on the other hand it was as 3:7 in the newly formed wood, and as 6:4 in the leaf-stalks, while in the flower-stalks it was as 2:9, and in the interior of the kernels of the ripe fruit as 2:7. Of all the mineral substances, sulphate of potash predominated in the leaves, and this was more especially the case in the spring, at the season of blossoming, whilst at the same period the juice of the bark and wood contained no trace of sulphuric acid. The ash of the leaves was very rich in insoluble phosphates, whilst that of the blossoms and fruit contained a larger amount of the soluble phosphates.

It is quite unnecessary to enter more fully into the question of the influence exerted by the alkaline and earthy carbonates, sulphates, and phosphates, upon the growth of plants as manure, for

this is a point which has been sufficiently proved by innumerable experiments, conducted both on a large and a small scale.

Now that we have acquainted ourselves with the different substances which contribute towards the nutrition of plants, and have discovered that they consist of a few very simple combinations, derived from inorganic nature, the question almost irresistibly forces itself upon our notice, *how the vegetable organism is able*, from these few substances, to generate such an *endless diversity of organic bodies?* But this, unfortunately, is a subject which admits of little more than mere conjecture. In conformity with the principles which we have adopted in this work of avoiding all diffuse discussion of subjective views, and carefully abstaining from useless hypotheses, we can only permit ourselves to examine some few of those conjectures, regarding the formation of organic matter in the vegetable kingdom, which admit of being referred to definite experimental facts. The number of such facts, however, is very small, notwithstanding the many laborious researches which have been made in relation to this subject by some of our most distinguished inquirers. Our general remarks on the study of the vital processes hold good in a higher degree for the processes connected with the formation of matter in the vegetable kingdom; for although we possess some few good isolated observations, we are entirely deficient in quantitative determinations, without which we can make no certain progress in our knowledge of the organic world. We are even ignorant of the relation existing between the carbonic acid which enters into the green parts of plants in solar light and the oxygen which is simultaneously given off. Yet how can we attempt to establish an hypothesis in reference to this process, before we have in some measure determined the numerical relations of the concurring substances? Very few numerical results have been obtained in phyto-chemistry, excepting some scanty determinations of Saussure, from which it would seem probable that about 2 parts of organic matter are formed in sunlight for every 1 part of absorbed carbon. Were we even able, chemically, to trace the qualitative and quantitative relations of the different substances in the order in which they originate in the plant, we should find that our very imperfect knowledge of the molecular forces, which play so important a part in organic processes, would prove very unfavourable to the comprehension of the chemical history of the gradual development of organic matter from such simple substances as carbonic acid, water, and ammonia. Whilst, on the one hand, the great simplicity observable in the

more delicate structure of plants, and the constant occurrence of certain substances such as organic acids, the so-called carbo-hydrates, and albuminous matters in all plants, without exception, seem to afford an explanation of certain phenomena; the endless variety of those secondary products, which are peculiar to almost every plant, throws such obstacles in the way of our inquiries that we can scarcely hope to give even a hypothetical representation of the formation of organic matter within the plant.

The entire vegetable organism is scarcely anything more than a system of cells, within which various substances are undergoing metamorphoses, and organic matter is passing through the earliest stages of its formation. The ammonia which penetrates into the roots, combined with sulphuric or carbonic acid, according to Liebig, or with humic acid, according to Mulder, must have passed through the cells of the fibrils of the roots. The decomposition of carbonic acid can only take place within the green cells of the plant, for the most torn leaf may continue to exercise the function of absorbing carbonic acid and giving off oxygen; but when once its cells are crushed or otherwise destroyed, this vital process ceases. Hence we are led to conclude, that in the cell-membrane, or, in other words, in the morphological relations of the cell, there is as important an agent for this process of metamorphosis as in the chemical character of the cell-contents. We have already frequently remarked that our present knowledge of endosmosis and diffusion is not sufficient to lead us to the correct interpretation of vital processes. Discoveries such as Graham's, that the chemical union of certain substances may be broken by simple diffusion, lead us to anticipate that many obscure points connected with these vital processes may be elucidated, and that we may at length be enabled to determine with some degree of accuracy, the results which would be produced by bringing heterogeneous matters in contact with a cell of certain dimensions, definite thickness of the cell-membrane, known contents, &c. At present we are only able to conjecture in the most general manner the mode in which certain physical and chemical processes are effected by the agency of cells. We are especially indebted to Mulder* for pointing out the various modes in which cell-formations may possibly contribute towards the vital economy of the plant.

We next pass to the consideration of the *formation of those non-nitrogenous substances*, which are common to all plants, and are especially characterised by containing, in addition to

* Vers. einer physiol. Chem. S. 781-791 [or English translation, pp. 716-725].

carbon, hydrogen and oxygen in the same proportion as they exist in water, and which have, therefore, received the irrational designation of *carbo-hydrates.* The first origin of these substances, which we meet with in their more advanced stages of development as dextrin, sugar, starch, and cellulose, has, with apparent correctness, been referred to the decomposition of carbonic acid under the influence of light. The opinion can scarcely be maintained in these days that the carbonic acid in the green cells of the plant is instantaneously decomposed, and that the separated carbon combines with undecomposed water to form dextrin, or sugar. Unless we have recourse to the direct intervention of a vital principle, or to some metabolic force of the cell, we must admit it to be highly improbable that the bonds which hold the oxygen and carbon in close combination should be suddenly rent asunder. As we are still very ignorant of the proportion existing between the absorbed carbonic acid and the exhaled oxygen, we can only regard the view as tenable in very general terms, that a decomposition of water is associated with a partial deoxidation of the carbonic acid. Liebig has indicated the special grounds which support the view, that the decomposition of water exerts an influence on the separation of oxygen during the action of solar light upon the leaves. Liebig's opinion that those organic acids which we meet with in various quantities in all plants, as oxalic, tartaric, citric, and malic acids, may be originally formed by the simultaneous decomposition of water and carbonic acid, gains a certain amount of probability from the confirmation or explanation which it furnishes in relation to several other facts. This hypothesis derives special support from the fact, that the alkalies occur in accurately limited quantities in plants, and especially in their green parts; for if only a definite quantity of certain bases is necessary to the life of the plant, we may readily understand that they will in the first place be employed for the saturation of the acids, and that when the acid by subsequent forces has been converted into dextrin, sugar, or other indifferent matters, the same amount of bases may again serve for the saturation of newly formed acid; and it may even be assumed that the alkali itself contributes towards the metamorphosis of the acid into these indifferent substances. We should find no lack of attempted explanations drawn from analogies of better known chemical processes, were we to advance further into the domain of pure hypothesis; but it must be borne in mind, in endeavouring to support such conjectures, that this process of deoxidation extends its

activity beyond the final generation of dextrin and similar neutral carbo-hydrates.

In addition to these substances, we find many which are widely distributed in the vegetable kingdom, and contain far less oxygen than the carbo-hydrates; as, for instance, the oleaginous fats, wax and resins, and several which are entirely without oxygen, that is to say, a large number of ethereal oils, caoutchouc, &c. When, moreover, we perceive that oxygen is given off, whilst carbonic acid is taken up, it would seem as if the developed oxygen were the combined result of the quantities of the gas yielded by several very different substances. Several phyto-physiological facts seem to indicate that the vegetable fats and wax are especially generated from the carbo-hydrate known as starch, whilst daily experience proves that those ethereal oils, which are either deficient in oxygen or entirely without that substance, can only be produced under the prolonged action of solar light. It is, therefore, not only not impossible, but even in some degree probable, that a number of different processes of deoxidation which extend to substances which have previously been more or less freed from oxygen, are simultaneously called into activity under the influence of solar light. Do differently constituted cells co-operate in these various reductions? Is it only one, or are there several matters which, under the influence of light, effect the elimination of oxygen from highly oxygenous substances? These, and numerous other questions of a similar nature, force themselves upon our notice, but, unfortunately, in the present state of our knowledge, they do not admit of satisfactory replies.

In considering the processes of deoxidation, which are connected with the life and growth of plants, we should bear in mind that some instances may occur in which the deoxidation is accompanied by a development of carbonic acid instead of a separation of oxygen. Liebig long since noticed during the prosecution of his experiments on fermentation, putrefaction, and decomposition, that oxygen was taken up by the organic substances during some of these processes of decomposition, and that then several atomic groups of carbonic acid were liberated from this combination. It depends entirely upon the relations existing between the oxygen that is absorbed and the carbonic acid which is developed, whether the remaining substance is richer or poorer in oxygen than the original body. If the volume of oxygen which is added be less than that of the carbonic acid which is evolved, the remaining org nic body will be less oxidised, and will therefore appear

as if it were deoxidised, exhibiting a decided process of reduction, notwithstanding the absorption of oxygen. Liebig made observations of this nature on the formation of carbo-hydrates from organic acids; if, for instance, 6 equivalents of oxygen be added to 6 equivalents of tartaric acid, and if 12 equivalents of carbonic acid are developed therefrom, we obtain grape sugar, which is relatively much poorer in oxygen ($6\,C_4H_2O_5 + 6\,O - 12\,CO_2 = C_{12}H_{12}O_{12}$). Starch might be similarly formed from tannic acid ($C_{18}H_6O_{10} + 8\,O + 4\,HO - 6\,CO_2 = C_{12}H_{10}O_{10}$). If more complete observations and experiments should enable us to prove that this kind of deoxidising process has a more general application in the vital economy of plants, many points might be explained which still present considerable obscurity; we might thus comprehend why, notwithstanding the reversed interchange of gases which takes place during the night, organic motion pursues its undisturbed course after the restoration of the less oxidised matters; that is to say, why the evolution of oxygen during the day is not exactly balanced by the nocturnal absorption of that gas. We need then no longer wonder that a plant may drag on a miserable existence in an inclosed space, since it generates for itself through the day the oxygen necessary for it during the night, and, conversely, exhales the carbonic acid during the night, which is again to serve for its nutrition through the day. This circulation of the oxygen is only apparent, for the oxygen which has been separated from its combination with carbon during the day, serves in the night to extract a larger amount of oxygen, together with some of the carbon of the organised matter. Thus we see by Erdmann's admirable experiments on *Tradescantia discolor*, that a plant may continue for years to vegetate in an unhealthy condition, although without entirely dying, when placed in a hermetically closed vessel. The death of some few leaves or stalks serves in these cases merely to prolong the life of the plant, and to promote the formation of new buds. The air within the inclosed space where such plants had for a long time vegetated, would at length become very rich in oxygen, if the above-mentioned parts, which die off, did not contribute by their decomposition to supply the new buds with carbon in the form of carbonic acid. If the nocturnal interchange of gases in plants depends upon the process to which we have here referred, the necessity of oxygen for the life of the plant would be obvious, and we should have a simple explanation of those experiments in which plants are found to vegetate in a non-oxygenous air only so long as the oxygen which is exhaled by

day is suffered to remain in the atmosphere surrounding the plant, and is not removed by the agency of chemical means.

It still remains for us to notice a hypothesis advanced by Mulder in explanation of the process of deoxidation in plants, as it leads us to the consideration of a point to which we have scarcely made a distant allusion in the above-mentioned hypotheses. As the property of absorbing carbonic acid and of exhaling oxygen is limited to the green parts of a plant, the idea naturally presents itself that the chlorophyll on which this colour depends plays a very important part in this process of reduction; although we are unable to decide, from the facts before us, whether the chlorophyll acts in the manner of a ferment, or whether this interchange of gases is dependent upon the formation of the chlorophyll from bodies richer in oxygen. Mulder has advanced the following hypothesis, which presents considerable plausibility. According to his view, new chlorophyll is always being formed under the influence of light, whilst the more richly oxygenous starch is simultaneously converted into wax, which is poorer in oxygen, wax being, as is well known, constantly present, together with the chlorophyll. On the other hand, microscopical observations of the development of cells and their contents render it very probable that granules of starch are gradually converted into globules of chlorophyll, which are rich in wax. Mulder supposes that the oxygen which is developed during the formation of wax from starch goes partly to the colourless chlorophyll, to convert it into the green variety, and that is partly given off, in a free state, to the surrounding atmosphere. Draper is more disposed to regard chlorophyll as a ferment, and he urges, as a proof of the decomposition of the (nitrogenous) chlorophyll, the above-mentioned fact that plants always develope some nitrogen in addition to the oxygen which they give off in solar light.

The *nitrogenous compounds* generally, and more especially those which are included under the term protein-bodies, play no less important a part in the life of plants than in that of animals; and there is no living cell in the plant which does not contain albuminous substances, either in the primordial utricle, or in some other form. Wherever the vital activity of the plant is most powerfully developed, the cells are found to be most richly endowed with these substances; as, for instance, in the fibrils of the roots, as well as in the flower and leaf-buds, in the pollen granules, in the embryonic sac, and more especially in the seeds. Although these local relations sufficiently indicate the importance

of these substances, they do not afford the slightest explanation of their mode of origin. Mulder does, indeed, conjecture, from the more abundant occurrence of these substances in the cells at the apices of the roots, that they are formed here from the ammoniacal compounds of the humus acids (as they are conversely decomposed into these acids and ammonia by the action of concentrated hydrochloric acid); but even if it be granted that the ammoniacal salts reach the plant only or principally through the roots, and if, further, it be shown that many of these absorbed substances undergo chemical metamorphoses in the fibrils of the roots, the frequent occurrence of ammoniacal salts in the rising sap of the plant seems rather to prove that their metamorphosis must be effected at some other point. It is not improbable that the protein-bodies are principally formed wherever the process of reduction is most practicable, as, for instance, in the leaves. On the one hand, we know that all protein-bodies, and especially those obtained from the vegetable kingdom, contain a considerable quantity of sulphur; and, on the other hand, we learn from E. Wolff's* carefully conducted ash-analyses of the different component parts of plants, that the sulphates, as already observed, are accumulated in early spring in the buds and leaves, whilst they disappeared from all other parts of the plant; and that the quantity in which they occur in these parts is too large to admit of the supposition that they are derived from the protein-substances already present in the leaves; we are, therefore, naturally led to the idea that the sulphates must be already accumulated in the leaves at a very early period, and that they undergo only a gradual reduction in order to be applied to the formation of albuminous substances in proportion to the quantity of ammonia with which the plant is supplied. We can hardly refer the deoxidation of the sulphates to any part of the plant except the leaves, and, on this account, we may assume that these organs afford the final stimulus required for the complete development of these salts. If it would not be carrying us too far into the region of conjecture, we might hazard the remark that as the alkaline carbonates contribute to the formation of non-nitrogenous bodies, the sulphates and phosphates may also take an important share in the formation of protein-bodies, such a conjecture deriving plausibility from the simultaneous occurrence of phosphates in all those vegetable organs which are rich in protein-bodies, and from the generally

* Journ. f. pr. Chem. Bd. 51, S. 1-82.

recognised importance of the phosphates in reference to the life of the plant.

Although there may be innumerable possible modes by which ammonia may be converted by the co-operation of other organic matters into albumen and vegetable gluten, we have not even the faintest support to offer in favour of any one or other of these hypotheses. The disappearance of ammonia, as such, from a compound, and its complete resolution into a new non-saline body, are familiar to the chemist, who—besides the metamorphosis of formate of ammonia into prussic acid and of cyanate of ammonia into urea—besides the formation of pigments from ammonia and orcine, phlorrhizine, hæmatoxyline, or erythrine—and besides the formation of alkaloids, according to Wurtz or Hoffmann—would call to mind innumerable instances in which the ammonia more or less lost its original character and assisted in forming new and very complex bodies, water being at the same time produced. But notwithstanding this pliability of ammonia, which enables it to incorporate itself with all forms of organic groups, we are wholly deficient in the facts necessary to afford special proof of the formation of a nitrogenous substance in the living vegetable organism.

When we have seen Dumas' beautiful idea, that organic nature generates its own elements, confirmed by the most recent investigations in the domain of theoretical chemistry, and now that we may look forward to the attainment of a more profound knowledge of the arrangement of organic atoms and of the internal connection of the endless number of organic bodies, through the brilliant discoveries of Kolbe, Hoffmann, Wurtz, Laurent, and others, and when, finally, the ingenious experiments of Liebig on fermentation and decomposition, on putrefaction, dry distillation, and other processes of decomposition, have enabled us to gain a deeper insight into the forms of the gradual regression of organic matter,—we may fairly hope that the time is not far distant when we may be enabled to trace the order of arrangement in which organic matter becomes fully developed. Then, too, we might hope to acquire a more intimate acquaintance with the requirements and circumstances under which the simpler molecules are accumulated and arranged into more complex atoms, until we might perhaps be enabled to form to ourselves as correct an ideal representation of the mode of origin of organic matter as we possess in reference to geological processes. But although the chemist may with pride refer to the great conquests he has

achieved in science during the last ten years, much yet remains to be done beyond what qualitative chemical experiments or even the most perfect theory of organic chemistry can supply; for notwithstanding the brilliant results attained in the science of phytotomy and phyto-physiology, we are still entirely deficient in exact experiments on the individual processes of vegetative life, we require a more perfect method of quantitative chemical analysis than we now possess, and we need scarcely make further allusion to our ignorance of the conditions and circumstances under which other molecular forces besides chemical affinity influence the metamorphosis and formation of matter in the vegetable kingdom. Yet notwithstanding the distance at which the aim of our inquiries presents itself to our notice, we are convinced that the time will soon arrive when that vital force, to which many have ascribed, together with chemical phenomena, an active participation in vegetable life, will be thoroughly eliminated, and when it will be finally laid aside, never again to become the subject of scientific consideration.

General Review of the Molecular Motions in the Animal Organism.

We have already (in the first volume) considered the material substrata of animal life, in as far as they can be separated by chemical means from the diversified group of substances which combine to form animal bodies, and can be tested and accurately determined by chemical reagents. We also endeavoured in the same portion of our work to estimate the value of each separate substance for animal life generally, as well as for the special purposes of life, after having considered its origin and ultimate disposition in the living organism, and indicated the position which it is entitled by its physiological importance to occupy amid this great number of chemical agents. It therefore only remains for us to notice in more general and more comprehensive terms the reciprocal actions of these individual parts during the vital activity of the organism, and their arrangement into a system of masses, constantly acting upon one another and inducing definite results.

In the second volume we turned our attention to the animal juices, which from their mobile and fluid nature have been

regarded by many as the essence and seat of all vital activity. In endeavouring to trace the intimate relations existing between these mutually allied substances from a chemical as well as a physical point of view, we were necessarily led to the consideration of the continuous metamorphoses which they had undergone during life, and of the causal connection of those phenomena which seemed to correspond with definite purposes in the living organism. It only remains, therefore, for us to take a collective and general view of the mutual relations in which the different juices stand to one another, the interchange of their constituents, and the dependence of the changes of any one upon another, or upon all the others, and thus to arrive at a general conclusion regarding those processes known as the metamorphosis of animal matter.

Finally, in this, the third volume, we have treated of the mechanical and chemical relations of the masses, which are consolidated into cells, fibres, and membranes, as far as this is possible in the present very imperfect state of our knowledge; and in these structures we have recognised not merely the hollow skeleton or framework between the parts of which the separate currents of these fluid masses move and circulate in uninterrupted motion in order to satisfy the different requirements of life, but we have also discovered in them the apparatus by which the most intense and peculiar actions of the animal organism are manifested.

Many might be led at first sight to suppose that we had accumulated a sufficient mass of materials from all directions to enable us to gain a deeper insight into the vital phenomena of animal life, or at all events to delineate in few but characteristic outlines the chemistry of the animal organism; but the more deeply we penetrate into the obscurity of the metamorphosis of animal matter, and the more carefully we investigate the materials in our hands, the more plainly do we perceive the deficiencies with which we have to contend. We have already frequently taken occasion to notice how little aid we have derived from previous scientific investigations in establishing general conclusions regarding any special group of animal molecular motions. It is therefore wholly unnecessary to enlarge upon these deficiencies, which we have already noticed in detail in the methodological introduction to the first volume (see vol. i., p. 8). We shall certainly not exceed the bounds of truth, if we maintain that we are still entirely deficient in the very first principles necessary for a scientific treatment of the theory of the metamorphosis of matter in the animal organism. It is merely to clear ourselves

from the imputation of exaggeration or the love of paradox in establishing this proposition, that we again refer to those points which we noticed under the head of Exudations (vol. iii., p. 123), and again in treating of the molecular forces which are active in the animal body (pp. 163–168), where the lamentable condition of our positive knowledge is too plainly showed. Qualitative analysis fails us when we attempt to investigate the different stages of transition and metamorphosis of the most essential substrata of the tissues in a state of change, whilst the extractive matters, in the absence of any rational explanation, have received the most various interpretations, in accordance with the imaginative ideas formed in reference to them by different observers. We have more than once admitted our fear that there is no speedy prospect of any great advance in qualitative chemical analysis, nowithstanding the light which various departments of this branch of science have derived from the genius of Liebig; and we have, on the contrary, expressed our conviction that it required numerous and more carefully conducted estimates of the quantitative relations of the constituents of the different animal juices, before the mechanical metamorphosis of matter could be placed on a sufficiently secure foundation to admit of our studying its chemical nature. We observed, in conclusion, that even the most exact measurements of the masses and velocities of the molecular movements of matter, in which vital activity is manifested, did not enable us to attain to a truly scientific theory of the metamorphosis of matter as long as we were constantly surprised by new and unexpected observations on the action of molecular forces. Even if we had mastered all the elements of this inductive inquiry, and could trace the mechanical and chemical features of the metamorphosis of matter, we should still be unable to comprehend the internal connection of the individual links of this great chain of phenomena—we should be unable to master the causal dependence existing between the different factors of vital motions—in short, we should be unable to give a *scientific explanation* of the mechanico-chemical processes in the living organism, until we had acquainted ourselves with the yet unknown laws of molecular forces.

Before we attempt to take a general review of the molecular movements in the animal organism, we think it will be expedient to add to the above remarks upon the formation of organic matter in the vegetable kingdom, a *comparison between the action of these forces* in the two great divisions of living bodies—the *vegetable* and *animal kingdoms*. A comparison of this kind has

frequently been attempted and carried out with more or less success, and pains have been taken to trace through their minutest modifications the differences presented by the specific methods of combination occurring in the two kingdoms, and the peculiar results of the individual forces manifested in these different spheres; but an exaggerated zeal for sharply defined distinctions of objects has frequently led to assertions which have rather tended to retard than advance the course of investigation. It almost seems like a satire upon Liebig's thoughtful researches, when we find the distinctions between the two kingdoms of nature laid down in such a manner as the following:—"The plant *generates* neutral non-nitrogenous bodies, such as fats, sugar, starch, and gum; *decomposes* carbonic acid, water, and salts of ammonia; *developes* oxygen; *absorbs* heat and electricity; is an apparatus of *reduction,* and is immovable. The animal *consumes* neutral non-nitrogenous bodies, such as fats, starch, sugar, and gum; *generates* carbonic acid, water, and salts of ammonia; *absorbs* oxygen; *developes* heat and electricity; is an apparatus of *oxidation,* and is movable." But nature will not be restricted within such narrow bounds, and in the teeming richness of her forms and phenomena, she speedily burst the bonds with which the human intellect capriciously attempts to restrain her.

Many of these distinctions are applicable when considered only in their most general bearings. The idea of a perpetual circulation in nature is most forcibly expressed in these two series. It is undoubtedly true that the organic matter which is generated in the vegetable kingdom is for the most part again destroyed in animals, but the idea that animals consume only protein-bodies, fats, and carbo-hydrates, and cannot also in part generate them, is an assumption which partly is false, and partly does not admit of proof. No one can any longer doubt that the animal body possesses the power of forming fat from other matters, such as protein-bodies or carbo-hydrates (see vol. i, p. 255). It yet remains an open question whether protein-substances may not also be generated in the animal organism under certain conditions, although it is most probable that such substances cannot be generated in the animal body (vol. i, p. 346). If we except the lower animals, we certainly are compelled to deny that the animal organism possesses the property of forming starch and cellulose; but sugar and dextrin are constantly generated within the bodies of the herbivora during digestion by the action of the saliva and pancreatic juice on the other carbo-hydrates (see vol. ii, pp. 31 and 114); and even in the bodies of the carnivora the liver has been recognised as a seat of

the formation of sugar, which most probably is solely produced from the metamorphosis of nitrogenous substances (vol. ii, p. 90), as I have recently proved by careful observations.* We must remember too what a number of substances are formed in the animal body which never occur in the vegetable kingdom. It has indeed been stated that these substances are only the products of a process of oxidation, but what an essential difference there is between xanthine or uric acid, and their homologues, theïne and theobromine! and who could determine, on seeing taurine or cystine, whether it were derived from the vegetable or the animal kingdom, if he were ignorant of the origin of these substances? Those complex substances, the biliary acids, have no analogues in the vegetable kingdom, nor can we deny to the animal organism generally the property of generating new organic matters within itself; but in this respect the animal organism is very much in the same condition as the chemist in his laboratory; both require, for the most part at least, ready-formed organic matter, from which to generate new substances foreign to, but analogous with the products of the vegetable kingdom. As many of the excreted matters of the animal body contain somewhat complex atoms of organic matter, the proposition that animals give off to the external world carbonic acid, water, and ammonia, is only half true: for although we regard the urine collectively as an ammoniacal salt, and even take the same view regarding the taurine of the solid excrements—and although, further, we comprise under the same head, and as of equal value with the carbonic acid and water, the formic, butyric, acetic, and caproic acids of the sweat—it yet cannot be denied that men and animals daily give off directly to the external world no inconsiderable amount of protein-bodies; since the solid excrements are never free from mucus, and since the desquamation of the epithelium and the abrasion of other horny tissues occasion a loss in these complex bodies, the amount of which may even be ascertained by moderately careful investigations.

It is also perfectly true that the vegetable cell, which is capable of overpowering the strongest chemical combinations, eliminates oxygen from the atmospheric ingredients, carbonic acid, and water, and is able to fix the indifferent substance, nitrogen, whilst the animal germ can only be developed by the co-operation of atmospheric oxygen. It cannot be denied that the separation of oxygen in the vegetable organism constitutes one of the principal momenta of chemico-vital activity, and that a progressive motion is induced

* Ber. d. k. sächs. Ges. d. Wiss. zu Leipzig, 1851, S. 130-164.

in the chemical molecules by the action of the vegetable cell, the object of which is to separate the oxygen as far as possible, and to restore the most complicated radicals (the most perfect organic matter), whilst the animal organism borrows this matter from the plant for the purpose of finding a main support for the most important animal functions in the regressive motion which the oxygen generates in the oxidisable matters. Hence it is true that oxygen is the exciter of animal life; through its agency the primary mucus or the plasma becomes converted into a cell, the cell is developed into fibre, and animal matter into the animal.

Yet however much truth may attach itself to such abstract assertions, we always find in association with the truth the germs of many errors. In treating of the formation of organic matter in the vegetable kingdom (p. 180), we noticed the concurrence of several processes of oxidation with the deoxidation going on in the plant; in like manner we also find in the animal organism, in addition to the oxidation in the blood of the capillaries, numerous processes of reduction, scarcely less intense than those which we meet with in plants; thus, for instance, in the primæ viæ we have seen that substances, such as sulphates, which require the most powerful agents for their reduction, were completely deprived of their oxygen (see vol. i, p. 445); that the oxides of iron and mercury, and similar substances, were deoxidised in the intestine; whilst we elsewhere drew attention to the fact that the fats and lipoïds, which are first formed in the animal body, can only be produced by a process of deoxidation. Even if we assume that oleic and margaric acids are formed from starch or sugar by such a process of cleavage as that by which alcohol is generated from sugar, (so that the reduction is only an apparent one, since the body is simply decomposed into one richer in oxygen, namely, carbonic acid, and into one poorer in oxygen, as alcohol, fusel oil, margarin, or olein); yet stearic acid, which is very rarely taken up by animals in vegetable food (hitherto it has only been found in cacao-butter), must be formed by a direct process of deoxidation, as both its composition and its chemical qualities show that it can only be regarded as a lower stage of the oxidation of the radical of margaric acid? Nor can we assume that a substance so poor in oxygen as cholesterin, which so readily accumulates in the stagnant fluids of the animal body, can be formed from the simple decomposition of some organic matter. The oxidising force of the animal organism is bounded by tolerably narrow limits; sulphide of potassium, when present in sufficient quantities, passes, in part, in an unoxidised form into the

urine through the blood which is so rich in oxygen; saligenin is not even converted into salicylic acid in its passage through the blood. We can scarcely refer cystine, which is so rich in sulphur, to any other source than a process of deoxidation; whilst the great amount of sulphur present in many horny tissues, which contain a perfectly identical group of atoms with albumen, can hardly be ascribed to any cause but a mere local deoxidation. If it be true that the iron contained in hæmatin may be extracted by sulphuric acid and water under the development of hydrogen, a reducing apparatus must be employed in some part of the animal body, by which the iron, which only reaches the body in an oxidised condition with the vegetable food, can be deprived of its oxygen. We shall meet with many other processes in the animal organism which, without intentionally setting aside the ordinary chemical terms, we can only designate as reduction-processes. Generally speaking, however, the restoration in the animal organism of bodies which are deficient in oxygen, is effected in a different manner from what is found to prevail in vegetable structures. Thus, for instance, in the formation of most of the fatty acids from sugar, a larger or smaller number of atoms of oxygen combine with the corresponding number of atoms of the hydrogen in the sugar, whilst a certain number of atoms of carbonic acid are simultaneously liberated, leaving a body which is always poorer in oxygen than the starch or sugar which was exposed to decomposition. We shall revert on a future occasion to this hypothesis, which was first advanced by Liebig, and which certainly appears to be confirmed by the most remarkable analogies with known processes of fermentation. In every case of the formation of a body poor in oxygen the animal organism presents greater similarity in its action to the chemical process of reduction than to the process going on in plants, by which oxygen is directly separated. As the chemist only calls into play other affinities of oxygen in order to remove it from certain combinations, so the animal body places the carbo-hydrates[*] in a circle of circumstances, under which other affinities of oxygen come into action, and give rise, as products of the process, to one of more comparatively non-oxygenous substances, together with a body rich in oxygen.

We shall pass over the other distinctions which it has been attempted to establish between plants and animals, as they are alike unstable and indefinite.

We will now include in one general *resumé* the leading propositions presented to our consideration by the three main divisions of physiological zoo-chemistry. If we pause for a moment to con-

template the great series of the chemical substrata of the animal body, we at once perceive that there are four principal groups of substances in which the vital processes are manifested with the greatest intensity. Amongst these the *albuminous substances* or the so-called protein-bodies, and their *derivatives* are the most conspicuous. A mere superficial glance at the occurrence of albumen is sufficient to show that this must be one of the most important substances in the whole animal body; we have met with it in the largest quantity in the blood, and in all those animal juices which contribute directly towards the nutrition of the organs, and a more careful examination of many of the animal tissues shows that albumen requires only some very slight modifications to become consolidated under different forms; as, for instance, when it contributes towards the formation of the solid contractile parts, under the form of syntonin (muscle-fibrin), by which alone both the voluntary and involuntary movements of the animal body are effected. We found it both in a dissolved and an undissolved form in the most delicate organic combinations, as, for instance, in the contents of the nerve-tubes—structures by which the animal essentially differs from the plant, and in which the highest force of all animal life may be said to be located. While we are compelled to admit that chemistry is still unable to furnish the long looked-for explanation of the internal constitution of albumen and of the substances most nearly allied to it, as syntonin, fibrin, and casein, or to trace the numerous morphological metamorphoses to which they are subjected, we are still less able to answer the question, wherein lies the capacity of these substances to preside over the highest functions of life. As long as the chemical questions regarding the difference of albuminous substances of identical or similar composition remain undetermined, we have no immediate prospect of solving the physiological problem of what it is which capacitates these substances for different vital functions.

We find that the animal germ is surrounded by albumen and casein, containing salts, together with a little fat and traces of sugar; hence it is to the albuminous contents of the egg that we must refer the development of the organs of animals, including even those structures whose substances do not appear very similar to albumen. Animals obtain during the period of lactation, besides fat and sugar, a substance which, with the exception of a smaller amount of sulphur, contains the same elements, and in the same proportions, as albumen; at the period, therefore, when the growth of the gelatigenous, non-albuminous tissues requires the largest supplies from without, the body is supported by the same

organic compounds which occur in such large quantities in its true nutrient fluid, the blood. Herbivorous animals do not find any substance analogous to gelatin in their vegetable food, and hence they must generate it from the albuminous substances of plants. All the solid bases of the animal organs consist of nitrogenous matters, which can only originate from the albumen, on which account we have named them derivatives of protein. Although we may entertain no doubt that the albuminous substances are gradually metamorphosed into the non-sulphurous constituents of the gelatigenous tissues through the agency of the oxygen which enters the blood, we are not able to advance anything beyond mere conjecture in reference to the mode in which these processes of metamorphosis are effected. We are still ignorant of the intermediate stages through which the albumen or the casein undoubtedly passes before it appears in the form of a chondrigenous substance, nor do we comprehend the internal connection, although the metamorphosis of chondrigenous into the glutigenous tissue takes place almost directly under our eyes. Although we may succeed in exhibiting the result of these metamorphoses by very simple formulæ, we do not by that means the more clearly determine the actual nature of the process.

The question whether the blood-fibrin constitutes the necessary transition-stage from albumen to chondrin and gelatigenous tissue, has been more than once propounded in the preceding pages (see vol. i, p. 396, and vol. iii, p. 137), and we might with equal justice inquire, whether the chondrin must everywhere precede the glutin in the formation of connective tissue, the tendons, the skin, &c.? A very simple scheme of these forms of metamorphosis might readily be deduced from a theoretical combination of the formulæ representing the composition of these substances; but even if we were accurately acquainted with the rational composition of all these complex substances from a chemical point of view, our ignorance of the individual conditions of the process would prevent our being able to decide with certainty which of the many possible combinations and modes of representation expressible in formulæ should receive the preference. We have here to inquire if *that* formula is the correct one, which imitates a process of decomposition (or indicates the metamorphosis) in which atoms of oxygen are added, and water and atoms of carbonic acid are abstracted; or whether the preference is due to that formula by which the substance undergoing metamorphosis yields known excretory substances in addition to the main product; or whether that is the

correct one which derives a new substance from the original one by the mere substitution of individual elements. There is one circumstance, however, which appears, at all events, to prove that the simplest chemical equation is not always the most correct in these processes, which seem to depend upon such highly complicated conditions. For, when we find that a concurrence of many different substances is necessary to the accomplishment of many processes, as, for instance, that nutrient matters are only imperfectly, if at all, digested without the presence of fat,—that no cell, fibre, or membrane can be formed without the presence of fat, phosphates, &c.,—we can scarcely suppose that a simple formula, based upon an unestablished atomic composition can express the true process of the metamorphosis. There are certain substances which never occur isolated in the animal organism during chemical metamorphoses; thus, for instance, wherever albuminous matters occur, non-nitrogenous carbo-hydrates are always present, however small may be their amount; wherever fats are formed or decomposed we always meet with albuminous matters; whilst free acids and alkalies occur in almost every part of the animal body. Although we may not admit the necessity of the concurrence of two or more entirely different substances in the case of individual processes, we rather conjecture that such a necessity obtains from the analogy of those processes which we are able to induce in organic substances that are not included in the sphere of vitality. We perceive very clearly from a study of the process of fermentation, that one organic substance cannot exist together with another undergoing the process of metamorphosis, without being implicated in an analogous molecular motion, corresponding to its constitution. May we not conjecture that the substances formed under these conditions possess the tendency to combine together in their nascent state, and thus give occasion to the formation of certain complex atoms, in which chemistry has recognised proximate constituents, conjugated compounds, haloid salts, &c.? It is here that the recent chemical theory of the substitution of certain elements by other more simple or compound molecules will find the most extended application, and where we shall discover new proofs of the generally recognised proposition, that nature, under all circumstances, accomplishes the most varied ends by the simplest means. Hence it would be difficult to prove, and indeed it appears almost improbable, that those nitrogenous matters which have less affinity with albumen, as for instance, the animal pigments, the resinous acids of the bile, &c., are the simple

remains of the decomposition of albumen or glutin; and, on several grounds, it might even be supposed that these matters have been formed from the products of the simultaneous decomposition of nitrogenous and non-nitrogenous bodies. The result of these considerations and of all the attempts made to explain the formation and decomposition of all these nitrogenous substances, keeps us within a circle of mere probabilities and possibilities, without affording any solid support for the maintenance of any one view in preference to another. The only fact which we deduce from a simple comparison of the empirical composition of these substances, and from corresponding statistical investigations regarding the metamorphosis of matter in the animal body, is, that the different phases under which nitrogenous molecules appear in the animal organism must be essentially dependent upon the inspired oxygen, and that the latter, under the most various circumstances, gives origin to the numerous metamorphoses which the molecules of albumen undergo before their final change into urea and similar substances.

In a second group of substances which we have learnt to recognise as important agents in the metamorphosis of animal matter, we must place the *fats*. We considered their physiological importance, origin, and final destruction so fully in the first part of this work, that very little remains to be said on the subject. We learnt (vol. i., pp. 259-272) that the fats, besides the manifold mechanical services which they render the animal organism, also take part, through their chemical metamorphoses, in the most varied animal processes, that they take an active share in the process of digestion in the primæ viæ, and that they preside generally over all the processes by which the fluid nutrient substances are converted into the solid substrata of the organs. The formation of the colourless blood-corpuscles seems also to owe its first impulse to the metamorphosis of fat, which thus serves as the most important auxiliary in the formation of blood. We also, in the same place, drew special attention to the fact, that no animal cell and no fibre was formed independently of the presence of fat. Indeed, the fat appears to possess the property of predisposing the animal organism to the formation of cells. Thus, for instance, whenever very large quantities of fat are introduced into the organism, as in the fattening of live stock, the connective and subcutaneous tissue of different parts exhibit an extraordinary number of cells, all which contain fat. A cell-formation of this kind requires, however, the concurrence of albuminous substances,

which are derived from the albuminates introduced into the organism with the food, as long as these are supplied in sufficient quantity. When the organism does not find in the food sufficient materials to form the investing membranes of the fat-cells, it borrows from the muscular fibre the substance with which it surrounds the fat in these protein-capsules. When this source of materials for cell-formation is no longer sufficient, the fat begins to accumulate in the blood and other animal fluids. These results were deduced by Persoz and Boussingault,* from a series of most carefully conducted observations on animals which were being fattened. A similar series of metamorphoses may be frequently observed in different morbid conditions; all the stages induced from excess of fat may be traced in the bodies of drunkards, for here a large amount of material forming fat is, as a general rule, introduced into the body, with only a very small quantity of substance that can be applied to the formation of cells; and in the artificial fattening of animals, the fat has the greatest tendency to collect in cells that are already formed, as for instance, in the liver, and this gives rise to what is termed the fatty liver—a morbid change which induces a certain group of disturbances. In short, we see that the fat, even considered from this point of view, stands in the closest relation to the formation of cells.

Whilst in the above-mentioned cases fat gives occasion to the formation of cells in the animal body, we see a tendency to the accumulation or new formation of fat in existing cells and tissues whose nutrition has been to a certain extent altered (see vol. i., p. 268). This tendency is most clearly manifested in those pathologico-anatomical cases which have been commonly known under the name of fatty degeneration. These frequently occurring phenomena may be interpreted in two different ways; for it may be assumed, either that the fat which is already present may be disposed by certain molecular forces to accumulate in the older and less vitally active cells, where it replaces the disappearing nitrogenous tissues; or that the fat arises directly from the nitrogenous substrata of the cells or fibres, and that their nitrogen disappears under the form of ammoniacal salts or other simple combinations, leaving fat as the secondary product of the decomposition of albuminous matter.

It must be observed, in reference to the latter hypothesis, that hitherto all attempts made to convert protein-bodies into true fat by chemical means have proved unsuccessful, although there is

* Ann. de Chim. et de Phys. 3me Sér. T. 14, p. 413-435.

nothing, in a chemical point of view, at variance with such an assumption (see vol. i, p. 258); indeed Liebig* has especially shown that it is not only possible, but also probable, in a chemical point of view, that the albuminous substances of the animal body may be converted into fat. We find that in the putrefaction, as well as in the gradual oxidation of albuminous substances, there are formed, in addition to butyric acid, a number of acids which belong undoubtedly to the group of the fatty acids, and are thus closely allied to the fats; indeed fat may, under favourable conditions, be converted into ammonia and such fatty acids (butyric and valerianic acids); hence it may fairly be assumed that under the peculiar conditions presented by dead cells and tissues in the living organism, the process of decomposition takes the same course in nitrogenous matters as in the butyric or valerianic fermentation of the protein-bodies, with only this difference, that in the former case, where there is only a small supply of oxygen, oxides having higher carbo-hydrogen radicals are formed. If the formation of adipocire were more carefully examined, we should find that it presented the most striking instance of a true fatty fermentation of albuminous bodies. Chevreul, as is well known, found saponified fats combined with ammonia and lime in adipocire, which led to the conclusion that the nitrogenous constituents of the muscles undergo the process of putrefaction during the formation of this adipocire, and that the ammonia which is formed combines with the fat existing during life to form soaps, whilst the greater part of the oleic acid is destroyed, or carried away, or converted into margaric acid. Recent experiments made by Quain† and Virchow‡ on the conversion of muscular tissue into adipocire in macerating troughs seem rather to give some weight to the older opinions, that it was not merely the pre-existing fat which was saponified in this process, but that the albuminous constituents of the muscles were separated into fatty acids and ammoniacal salts. This subject requires, however, to be more carefully investigated before we can venture to decide to which of these hypotheses we ought to give the preference.

Virchow§ has long been one of the most zealous supporters of the view that albuminous substances are converted into fat *within the living organism.* This observer was the first pathological

* Chem. Briefe. 1851, S. 491 [or Letters on Chemistry, 1851, p.379.]

† Medico-chirugical Transactions. 1850, Vol. 33, p. 141.

‡ Verh. d. phys.-med. Ges. z. Würzburg. Bd. 3, S. 369.

§ Arch. f. path. Anat. Bd. 1, S. 30-64.

anatomist who studied the so-called fatty metamorphosis in certain cellular organs, as for instance, the kidneys, spleen, liver, &c., and recognised it as one of the more frequent terminations of the process of inflammation, whilst Schultze* regarded it as the product of excessive plastic activity (see vol. i., p. 252). Virchow has attempted, with considerable ingenuity, to show that an accession of fat from without is scarcely conceivable during the fatty degeneration of entire organs and individual cells; but still we can hardly consider this view fully proved, owing to the extensive diffusion of fat in most animal fluids, and the frequent depositions of fat in organs enlarged by morbid processes. The interesting experiments of R. Wagner† appear, however, to furnish the most decisive proof in favour of this view. When Wagner found that testicles which had been introduced into the abdominal cavity of hens were completely changed and converted into a shrivelled fatty mass, he introduced crystalline lenses, portions of coagulated albumen, and similar non-fatty protein bodies into the abdominal cavities of pigeons and other birds, and these, after a lapse of time varying from twenty-five to fifty-four days, were also found to be wholly changed, leaving a residue, the quantitative analysis of which yielded, in addition to some traces of nitrogenous matters, a larger proportion of fat than the substance originally employed had contained. Donders‡ and Middeldorpf§ have subsequently made similar experiments with tendons, cartilages, and bones, and obtained very nearly the same results as Wagner; Donders, however, maintained that the fatty metamorphosis must be limited to the cells; but this opinion seems to be refuted by the observations of Wagner and others. As, however, Wagner himself had started the objection, that fat might be introduced from without, that is to say, from the exudation forming itself (from fat) around the foreign body, and might pass into the disappearing nitrogenous matter, more especially as in some, although not in all cases, the fat presented the appearance of having been infiltrated from the external surface, it was necessary to alter the experiments by cutting off every supply of fat from without. For this purpose Husson,|| who had repeatedly confirmed Wagner's earlier observations, undertook a series of experiments under the direction of

* De adipis genesi pathologica, Comm. præmio orn. Gryphiæ, 1852, p. 47.

† Göttinger gel. Anz. 1851, No. 8.

‡ Nederlandsch Lancet, 3 Sér. Jaarg. 1, p. 556.

§ Günsburg's Zeitschr. f. klin. Med. Bd. 3, S. 59.

|| Göttinger gel. Anz. 1853. No. 5.

that physiologist, introducing into the abdominal cavity of pigeons portions of albumen or crystalline lenses enclosed in gutta percha bags. These experiments, in which there was only a very small increase of fat where the gutta percha bags were well preserved, seem rather to speak against the formation of fat than to confirm such a view. Schrader* employed crystalline lenses inclosed in stoppered glass tubes for similar experiments: he did not, however, make any quantitative analyses, but merely thought he had discovered the presence of fat by examination with the microscope. F. W. Burdach† has recently carried on some very circumstantial experiments, in which according to Wagner's method, portions of albumen or crystalline lenses, inclosed in collodion or caoutchouc, were introduced into the abdominal cavity of animals, and examined after an interval of a month or even a longer period of time; from these observations Burdach convinced himself that where the animal juices were entirely cut off, the protein-body was not metamorphosed into fat, nor did it undergo any essential alteration from the simple action of the animal heat; whence it followed that if the protein-substances are actually converted into fat within the animal body, the free access of animal juices is at all events indispensable to the process. Burdach also found that when the albuminous substances were enveloped in collodion, a very fatty yellowish layer of exudation was formed upon the latter, in consequence of the exudative inflammatory process, in precisely the same manner as when such a mass is deposited directly upon the protein-substance. It is, therefore, obvious that the yellow fatty rind observed in Wagner's experiments is not the result of the decomposition of the protein-substance, although it is possible that the whitish fat which appears as if infiltrated into the object (but seems to be always more copiously deposited on the circumference than at the centre) may derive its origin from the decomposition of the protein-body. With the view of determining this question, Burdach employed porous vegetable matters, such as wood and elder-pith in place of the protein-substances in his experiments, and the results obtained were very nearly the same as those observed in the case of nitrogenous animal matters, the yellow fatty exudation being deposited round these substances, and the fat having been imbibed, through the intercellular spaces of the periphery, into the innermost part of the wood or elder-pith.

* Göttinger gel. Anz. 1853. No. 5.

† Dissert. inaug. med. Regimontii, 1853.

As this method did not afford any prospect of deciding the question of the formation of fat from protein-substances in the animal body, Burdach has attempted another method, which, as far as we are able to judge at present, appears likely to furnish definite results. Comparative analyses of undeveloped and already developed ova have been instituted, with a view of ascertaining the increase or decrease of certain salts or of sugar during the development of the embryo; and the first question which presents itself for consideration is whether the embryo does or does not contain more fat and less protein-bodies than the egg from which it is developed. If the amount of fat in the egg increased in a definite ratio to the diminution of the protein-substance, or of the nitrogenous matters generally, the conversion of protein-matter into fat during the metamorphosis of matter would be demonstrable at all events for this case. Burdach certainly found in some experiments which he made on the ova of the Limnæus stagnalis, that there was no inconsiderable increase of fat during the development of the embryo; but as these few observations did not coincide perfectly as to their results, the question must still be regarded as undecided.

The third group of the most important substances of the animal body (comprising the *carbo-hydrates*) stands in such an intimate relation to fat, that in noticing these bodies we shall at the same time have occasion to make many additional remarks regarding the value of fat in the animal economy. We are only acquainted with four substances of this group as constituents of the animal body, namely dextrin, milk-sugar, inosite, and grape-sugar (glucose). We have already seen that the carbo-hydrates (with the exception of the cellulose deposited in the outer integuments of the Tunicata, (see vol. i. p. 299) never constitute the basis of tissues. Sugar which was formerly considered to be almost limited to the primæ viæ, has recently been discovered in nearly all the animal fluids which contribute towards nutrition, such as the blood, the transudations, lymph, chyle, the white of egg, &c. The sugar which we find in the intestinal canal of the herbivora and omnivora owes its origin to the metamorphosis of the starch and other carbo-hydrates through the influence of the saliva and pancreatic juice; but sugar is also met with in no very inconsiderable amount in the blood of the carnivora (see vol. ii, p. 211), and must, therefore, be dependent upon some other source besides the carbo-hydrates which are introduced into the body from without. I have been enabled by a number of comparative analyses of the blood of the

portal and hepatic veins to give considerable probability to the view,* that the sugar which is formed in the liver—a fact which was originally discovered by Bernard, and subsequently confirmed by Frerichs (see vol. i. p. 290, and vol. ii. p. 90)—owes its origin to the decomposition of albuminates, and more especially of fibrin. The possibility that a carbo-hydrate may be contained in albuminous substances as an intimate constituent or adjunct, as in salicin, phlorhidzin, and amygdalin, was first conjectured by Berzelius, and has since been clearly demonstrated by Liebig. The tendency of albuminous substances to pass into the butyric fermentation, which is especially noticed in fibrin and casein, may also, perhaps, be interpreted in the same manner. Hence not merely the sugar which is conveyed into the bodies of herbivorous animals with the food in the form of starch, but especially that which is generated in the organism itself, must possess high importance in the metamorphosis of animal matter generally. It is a striking fact, however, that notwithstanding this abundant supply both from without and from the liver, sugar is found only in comparatively small quantities in the blood of herbivorous animals, although it is present in scarcely smaller quantities in the blood of the carnivora, even after the use of a purely animal diet. It is not less remarkable that nature has provided the egg with a small quantity of sugar, and that the amount of sugar in the hen's egg is increased rather than diminished with the development of the embryo. These facts undoubtedly indicate that the sugar or the carbo-hydrates generally, as well as the fats, must serve some other purpose than that of maintaining the heat of the animal body by their simple, although gradual oxidation. It will be presently seen that by these remarks we do not by any means intend to deny that the development of the heat, which is generated by the consumption of these substances, is one of the most important objects of their introduction into the animal organism; but if the sugar served solely to generate heat, we can scarcely explain why the quantity should increase in the egg during incubation, whereas we should rather expect that it would wholly disappear during the oxidation which accompanies this process of development. The question further arises, why the sugar, which is certainly present in far smaller quantities in the blood of the carnivora than in that of the herbivora should not be immediately consumed in the former, and rendered unamenable to our reagents, since the sugar occurring

* Ber. d. k. sächs. Ges. d. Wiss. 1850, S. 130-146.

in considerable quantity in the herbivora is so rapidly removed from the blood either by respiration, or where this is inadequate for the purpose, by the urine (see note to vol. i, p. 293, in the Appendix).

We are still very imperfectly acquainted with those carbo-hydrates and their metamorphic products which occur in the animal juices; but it is very probable that in addition to Scherer's inosite, we may find other similar indifferent substances amongst the extractive matters of the animal body. We are, however, acquainted with many of the acids which are formed in the animal body from the carbo-hydrates, as for instance, formic, acetic, and butyric acids, which occur in large quantities in the sweat, and, in addition to these, lactic acid, which is associated with them in the muscular juice, in the parenchymatous juice of the smooth muscles of the stomach, of the intestinal canal, and of the bladder, as well as in the middle arterial coat.

We have already seen that in the small intestine free acid is commonly found as far as the middle of the ileum, notwithstanding the access of pancreatic juice and bile; here its use is assuredly not merely to dissolve the nitrogenous substances which were not digested in the stomach, but also essentially to promote the resorption of the soluble constituents of the chyme. The admirable experiments of Jolly* have shown us, that the endosmotic equivalents of the acids are extremely small, as compared with the equivalents of the alkalies, for he found the equivalent of hydrated sulphuric acid = 0·350, but that of hydrated potash = 215·725, and Graham† found the diffusibility of the acids extremely great, and that of the alkalies very small; it, therefore, stands in an inverse relation to the endosmotic equivalents. Graham observed amongst other things that an acidified albuminous fluid was much more diffusible than an alkaline solution of albumen. Whenever, therefore, an alkaline and an acid fluid are separated by a membrane, the main current of the interchanging fluids will always be directed towards the alkaline side, and hence it is most obvious that the acid of the small intestine must aid in essentially promoting and facilitating the resorption of the contents. There can therefore be no doubt that the carbo-hydrates, or rather their acid products of metamorphosis, control some important function in the intestinal canal which does not stand in any direct relation to the process of respiration. We need hardly have recourse to

* Zeitschr. f. rat. Med. Bd. 7, S. 83-147.

† Ann. de Chim. et de Phys. 3 Sér. T. 29, p. 197-229 [or Phil. Trans. for 1850, p. 1.]

facts well known to the physician to prove the truth of this proposition, since the phenomena of indigestion in gastric catarrh, and the temporary benefit derived in these conditions from the use of acids are now explained by these purely physical relations.

This proposition acquires still higher importance in reference of the animal functions, when we consider the antagonism of the reactions of the different animal fluids, a condition which we shall more fully consider at a future page. We will here simply observe, that we find, when we examine the mixture of the animal juices already noticed, that on the one hand the free acid is associated with phosphates and potash-salts, and on the other hand a strongly alkaline reaction with soda-salts and chlorides. These occurrences are not the result of accident, and Liebig, as we shall presently see, has with his usual ingenuity and success elucidated the object and necessary results of this peculiar grouping of the acid and the alkali, and of the different salts in the animal organism. If we attend only to the constant difference in the reactions of the different juices, we shall have to admit, that the alkaline nutrient fluid of the blood must, in accordance with this physical law, transude far less readily than the acid parenchymatous fluids through the walls of the vessels. Even if the remarkable play of affinities in the phosphate of soda might often give rise to an acid reaction, such an effect could scarcely be produced unless carbo-hydrates were introduced into the body, or generated within it, by whose conversion into acids a part of the base would be abstracted from the phosphates taken with the vegetable food in order to convert them into acid salts, until the alkali, after being freed by combustion from its organic acid, might recombine with the phosphate.

If we deny this function to lactic and other organic acids, we could not admit the occurrence of an acid reaction, or what is the same thing, the formation of an acid phosphate in the organism, if the carbo-hydrates, without forming acids, were consumed in the same manner as in our furnaces or crucibles. The ash of plants always exhibits an alkaline reaction (excepting in the case of some seeds), and consequently the food of herbivorous animals could only generate alkaline fluids within the body if the carbo-hydrates were not, partially at least, converted into acids, and distributed with the phosphoric acid amongst the bases, thus serving to restore the acid salts and the acidly reacting fluids. Nature has, therefore, provided by this beneficial distribution of acids and alkalies for the removal of all effete matters from the tissues in the most rapid manner, and for their transference to the blood, where

they are employed in maintaining animal heat, or are entirely removed from the body with the urine and sweat, whilst on the other hand equally efficient means serve to render the passage of deleterious matters from the blood into the parenchyma of the organs extremely difficult, and to facilitate in an equal degree their expulsion from the organism by the aid of the urine and sweat.

Moreover, the carbo-hydrates, or rather the sugar, may very probably accomplish some other less striking functions before their conversion into acids; thus for instance, the sugar in the alkaline fluid of the blood certainly contributes its share to the solution of the carbonate and phosphate of lime, as is very obviously manifested in the development of the embryo in the egg of the bird. It long remained a mystery to the older observers, how the salts of lime could be augmented in the embryo, and it was believed or assumed that the lime must be derived solely from the shell of the egg; but even if some acid salt of lime may be formed during the period of incubation, and may pass into the juices of the developed germ, yet the sugar, when present, combines with the alkali or lime in the alkaline fluid, and may then dissolve the carbonate of lime as a compound of sugar with lime or soda, a fact which has been long known and has been recently brought to notice by Barreswil.* May not the capacious size of the liver of the chick during the latter days of incubation be the cause of the greater amount of sugar which is found in the albumen of the egg at that period than before incubation? And may we not conjecture that the liver of the fœtus of the mammalia, which, notwithstanding its size, secretes very little bile, may serve to generate sugar from the protein-bodies? This sugar, which I have determined with the greatest exactness in the fœtal blood of calves, is assuredly not formed in the liver simply to be consumed, for even if the albuminous substances in the fœtus are partially appropriated to the maintenance of internal heat, they would hardly be first decomposed into sugar and other substances in order to effect this purpose. The fœtus, which requires sugar quite as much as the young animal during lactation, generates it in the organs designed for that purpose, and the blood of the fœtus with its small amount of alkali has less tendency to decompose sugar than the more alkaline blood of breathing animals (see vol. ii. p. 255).

We have already frequently referred to the application of sugar to the formation of fat, and we will, therefore, simply observe that

* Moniteur Industriel. 1850, No. 1542.

according to Liebig,* the formation of fat from sugar may be explained in two different ways. It may in the one case be analogous with vinous fermentation, or with the formation of fusel oil, the atom of sugar being decomposed into carbonic acid, and into a substance poor in oxygen; or in the other case, the sugar may undergo a process analogous with the butyric fermentation, by means of which the hydrogen is in part abstracted from the carbo-hydrate, and carbonic acid escapes, while a substance poor in oxygen remains in the form of one of the known fatty acids. In the butyric fermentation, one atom of sugar is decomposed into hydrogen, carbonic acid, and butyric acid ($C_{12} H_{12} O_{12} = 4H + 4CO_2 + C_8 H_7 O_3 . HO$); in the formation of caprylic acid within the animal body, two atoms of sugar become decomposed into the above-named acid, carbonic acid and hydrogen, the latter combining to form water with the oxygen which it meets with in the blood ($C_{24} H_{24} O_{25} + 4O = 4HO + 8 CO_2 + C_{16} H_{15} O_3 . HO$). Liebig adduces an interesting experiment in support of the view to which we have already referred, that the formation of fat is effected in the liver. When pieces of calves' liver are chopped up in water, and suffered to stand at a temperature of 39° or 40°, an extraordinary amount of pure hydrogen gas will be developed in about four or five hours; some ferment must, therefore, be developed here, which is capable of separating the hydrogen from the oxygen. In every case the deposition of fat within the animal body betrays a certain deficiency of oxygen, showing that the amount of oxygen respired was insufficient to allow the complete separation of the sugar into water and carbonic acid.

The part taken by the *fats* in the metamorphosis of animal matter has already been very fully considered in the first volume. We there showed (after discussing the mechanical objects fulfilled by the fats in different parts of the animal body), that these substances accomplish definite purposes in the primæ viæ, and that they appear to be powerful auxiliaries in the formation of cells and tissues, whilst their ample supply of carbon and hydrogen, and their gradual oxidation, enable them to contribute essentially towards the generation of animal heat. We shall refer in a future page to the special value of the fats in relation to the generation of heat.

We now pass to another group of substances, whose occurrence in the body, and whose importance in the animal economy have already been considered in detail in the first volume of the present

* Thierchemie. 1846, S. 102. Chemische Briefe. 1851, S. 486-492 [or Letters on Chemistry. London, 1851, p. 377.]

work. On taking a general retrospective view of the substances which occur in the ash or which we assume to exist preformed as *inorganic salts* in the animal juices, certain general considerations which we have not hitherto noticed demand our attention. We have frequently had occasion to refer to the numerous defects which still appertain to the chemical analysis of the incombustible constituents of vegetable and animal substances, and which necessarily oblige us to exercise great caution in applying the results of ash-analyses to the explanation of the physiological actions of the substances which are found preformed in the living body. It is sufficiently evident, however, that these substances play a very important part, and that notwithstanding these defects in our analytical methods, they are more accessible to exact investigation than any other constituents of the organism. If any doubts still exist as to the necessity of their presence for animal life, we need only refer with Liebig to the series of experiments instituted by French investigators, in which animals were destroyed in more or less brief periods of time when fed upon substances containing no salts, although otherwise nutritious. We also learn from other experiments, in which animals were fed on substances which were deficient in certain mineral constituents, that a certain group of these bodies contributes essentially towards the nutrient power of the different articles of food. Liebig has especially drawn attention to this obscure and much neglected question, which he has made the object of numerous experiments, and has again recently studied, with his accustomed care and completeness,* ably elucidating the numerous relations borne by these substances to individual processes, as well as to the entire economy of the animal organism.

It is a singular circumstance that it should have been reserved for our own day to define with greater exactness the inequality in the distribution of the *free acid* and of the *alkali* in the juices of the animal body. Andral,† who was the first to institute observations in relation to this subject, prosecuted the inquiry purely in relation to medical diagnosis, and hence they did not yield any actual benefit to physiology; here, too, Liebig was one of the foremost in the field. If we revert to the experiments on the different animal juices described in the second and present volumes of this work, we shall perceive that the blood constitutes the main representative of those animal fluids which are distinguished by a

* Chemische Briefe. 1851, S. 495-544 [or Letters on Chemistry. London, 1851, pp. 382-440.]

† Compt. rend. T. 26, p. 650-657.

decided alkaline reaction, whilst the juices of the most vitally active organs have a decided acid reaction. Besides the blood, there are only few of the animal fluids which are constantly alkaline, as, for instance, the lymph, the chyle, and the transudations. Among the secretions, the saliva alone exhibits a strongly alkaline reaction under certain physiological conditions, whilst the bile and the pancreatic juice are so slightly alkaline that they are often unable, under ordinary conditions, to neutralize the acid masses which enter the duodenum from the stomach. On the other hand, we know to what a degree the gastric juice is distinguished for its acidity, and that the acidity of the muscular juice varies directly with the activity of the corresponding organs; the most recent experiments of Du Bois Reymond and Liebig showing that the muscles, when at rest, contain no acid juice. The parenchymatous fluids of the spleen, the thymus gland, the smooth muscles, the liver, and the supra-renal capsules, all contain free acid. This antithesis in the preponderance of the alkali and the acid is not only apparent in the mass of the coarser organs, but shows itself on a close examination even where we should not expect to meet with such differences, as for instance, in the egg and the blood. Although the fluid of the yolk exhibits no acid reaction towards vegetable colours, yet it is found, on a closer examination, to differ essentially from that of the white, which is so rich in albuminate of soda and alkaline carbonates as always to colour turmeric brown, whilst the yolk-fluid is so poor in alkalies that the casein contained in it is separated in granules. We might certainly regard this casein as the free acid of the yolk, if the ash-analyses of the latter did not show that the mineral bases are insufficient to saturate half of the phosphoric acid contained in it (see vol. ii, p. 360). In examining the blood, we find that a difference exists between the serum and the blood-cells precisely similar to that which we have noticed between the yolk and the white of the egg. If we are not mistaken, C. Schmidt has somewhere suggested that the contents of the red blood-cells may have an acid reaction; the numerous experiments which I have made in relation to this question have not enabled me to arrive at any definite results; but if we consider the composition of the mineral constituents belonging to the blood-cells as first determined by Schmidt, and if we bear in mind the facts* which have been recently established regarding the behaviour of the crystalline substance of the blood, its acid reaction on coagulation, the amount of

* [See note to vol. ii, p. 185, (on *the crystalline matter contained in the blood-cells*) in the Appendix.]

metaphosphates which it contains, &c., it becomes highly probable that the contents of the blood-corpuscles have either an actually acid reaction, or that, analogously with the yolk-fluid, they contain substances which are able to saturate the alkalies.

When we consider all that has been ascertained in reference to the nature of the free acids in the different animal juices, and all that has been set forth in different parts of the present work, we find that wherever free acids occur in the parenchyma of the organs acid *phosphates* are invariably present, or that where an acid reaction cannot be directly recognised, phosphoric acid is always met with, either conjugated or simply combined with casein, globulin, or glycerine. The proposition may, therefore, be established for all animal juices, which are neither secretions nor excretions, that in all juices which exhibit an acid reaction the soluble phosphates are especially accumulated, for it has been found that whenever the mineral constituents were determined by the ordinary method of incineration, the ash of all these juices, whether they exhibited an acid or a neutral reaction, was much richer in phosphates, and especially metaphosphates, than the ash of alkaline animal juices. As all these juices naturally originate in the blood, it would appear very singular, although by no means incomprehensible, that certain of these juices, as for instance the muscular juice, and the fluid bathing the contractile fibres, should exhibit such a strongly acid reaction if free organic acids and their alkaline salts were not also simultaneously present with the acid phosphates. This free acid, which as we have already seen, consists essentially of lactic acid, together with a smaller quantity of volatile organic acids, is originally generated in the parenchyma of the organs by their own functions, and the neutral phosphate which has passed from the blood is here first converted into an acid phosphate; such at all events is the case with the muscles, which Du Bois found to be without free acids when in a state of rest. We are, therefore, disposed to adopt the view advanced by Berzelius many years since, that this acid reaction is not the requirement, but the result of the function of the muscles.

Moreover the earthy phosphates are also brought into solution in larger quantity by the occurrence of free acids, than would have been the case by albumen or casein alone. It need not, therefore, excite our surprise, if we find large quantities of these phosphates present in the ash of the animal juices, for such a fact would at first sight appear to be the mere result of a chemical necessity; but we have already shown that although no free organic acids are formed anew in the parenchyma of the organs, the occurrence of

acid phosphates in them, although striking and inexplicable, is yet not inconceivable. After the wonderful discoveries of Graham in reference to these complicated endosmotic phenomena, which have hitherto been so imperfectly reduced to definite laws, we need no longer be surprised when we see an acid fluid separating from the alkaline blood, or an acid phosphate separating from the neutral phosphate, and permeating the coats of the vessels. A similar view must be taken of the faintly acid or neutral fluids in which, at all events at present, no organic acid has been recognised, as for instance, the yolk and the contents of the blood-cells; for it is certainly not very probable that these adjuncts, or faintly acid bodies, such as casein or glycerine, should be capable of decomposing the neutral alkaline phosphate.

We must here refer to an observation which is intimately connected with the above-described facts, and which bears upon the influence of these unknown laws of diffusion and endosmosis; we allude to the fact first observed by Liebig during his investigation of the muscular fluid, and subsequently confirmed by C. Schmidt in his investigation of the contents of the blood-corpuscles, namely, that these fluids, which are so rich in phosphates, and which exhibit an acid reaction, contain only a small amount of soda-salts and alkaline chlorides, while they are very rich in potash. This observation I have been able to confirm (see pp. 71 and 87) in examining the parenchymatous juice of the different contractile tissues; for I found that acid sweat, which was almost entirely free from phosphoric acid, contained a much larger quantity of potash-salts than were contained in the alkaline animal juices, which were richer in phosphoric acid. The experiments hitherto made on endosmosis and diffusion have indeed afforded some indications of the readiness with which the potassium-compounds transude, although they have not yielded any more precise results; Graham's* most recent experiments have merely demonstrated that hydrated soda and the soda-salts in general are diffused somewhat more strongly than hydrated potash, and the corresponding potash-salt. Here again, therefore, we are deficient in the elements necessary to furnish an explanation of these phenomena; that is to say, we are ignorant of the physical laws, whose application to organic nature, and whose utility in proving that all vital phenomena are results of a physical necessity, constitute the true essence and the ultimate aim of physiological chemistry and physiology. As long, therefore, as we continue in ignorance of the leading physical premises, we should

* Chemical Gazette. 1851, pp. 256-258.

abstain from having recourse to less efficient agents, such as nervous force and electrical endosmosis (although, as Du Bois Reymond has shown, these are not without their influence); least of all, however, should we conceal our ignorance by calling to our aid any peculiar vital forces.

But if we do not regard the occurrence of free acids, acid phosphates, and an excess of potash-salts as purely accidental, in so far as we recognise their presence as *the result of a necessity*, that is to say, as the effect of physical laws, we are also equally bound to consider that their presence may not be accidental when examined in a teleological point of view; that is to say, we ought also to inquire what purposes are accomplished by the occurrence of the free acid, the phosphates, and the potash-salts in the fluids of these organs; or rather, what effects are necessarily produced by the presence of these substances in the organs under consideration. The present state of our knowledge does not, however, enable us to decide this point with more certainty than we have already indicated in the first volume, when treating of lactic acid and the phosphates. We are entirely unable to conjecture the effect which may be produced by the simultaneous presence of the phosphates and potash-salts on the metamorphosis of matter, either in the organs or in the surrounding parts; for mere surmises and hypotheses regarding polar antitheses, and the like, call for no further notice till we are more conversant with the effects of polarity.

There is, however, one point of view which must not be wholly neglected in our considerations of the antagonism of the reactions, and of the different salts occurring in these organs and in the blood, since it may, in this respect, possibly present the idea of an antagonism between the organ and the blood under such an aspect as to necessitate our relinquishing it entirely. Here, for instance, the question especially arises, whether the acid reaction and the amount of phosphates in the fluids are solely dependent upon the quantity of fibre-cells or smooth muscular fibres contained in the organs, or whether they are definitely associated with the organs as such. This question must certainly be answered before we enter into further discussions or investigations, since so many facts appear to show that this free acid, and this abundant supply of phosphates and potash-salts, which we have found to be the constant associates of the smooth muscular fibres, occur in the various organs solely in proportion to their number of contractile fibre-cells; we need here only refer, by way of illustration, to the fact, that organs, such as

the spleen and the muscular layer of the intestinal canal, which are especially rich in contractile tissues, are also especially distinguished by the amount of free acid, &c., which they contain; whilst, on the other hand, the juice of the salivary glands and of the pancreas, in which Kölliker discovered few or none of these fibre-cells, are distinguished by their alkaline reaction and by their poverty of potash-salts. I have ascertained from direct observation that the middle coat of the aorta and the A. innominata yields far less acid, phosphates, and potash, in proportion to the amount of fibre-cells, than the same tissue from middle-sized arteries. It requires, therefore, further and more exact investigations to determine whether the juice of the spleen and similar organs exhibits an acid reaction, &c., simply because it is blended with the juice belonging to the fibre-cells, or whether the presence of these substances is inherent in the organ as such; but still it must be confessed, that our histochemical investigations render the former view by far the more probable.

We likewise meet with accumulations of *phosphates* independently of the presence of free acid, or the formation of acid salts, in parts of the animal body where their presence has either served certain definite purposes, or where it is still regulating certain functions; instead, however, of recurring to the observations we have already made in relation to this subject (see vol. i. pp. 412-418 and 440), we will here merely refer to the following facts. All histogenetic substances are almost inseparably combined with considerable quantities of phosphates, so that the two are always dissolved together, and are again associated in all coagula or precipitates obtained from their solutions. The bases of all completely developed tissues always contain in their ash considerable quantities of phosphates, which for the most part are in the proportion of 1 equivalent of phosphoric acid to 1 equivalent of base, and therefore occur as metaphosphates; as for instance, in the case of the muscular substance, and the substance of the connective tissue of the lungs and of the liver, after being thoroughly rinsed in water according to Liebig's directions. Hence we may conclude, that acid phosphates must have been present in the recent tissue, or rather that a portion of the phosphoric acid was combined with organic matters. We have further seen (see p. 135) that all secretions from the blood, which are distinguished by their plasticity, exhibit phosphates, which although not always present in large quantities, never fall below a certain amount; and the admirable observations of C. Schmidt have shown that a certain quantity of phosphates is

required to supply the first basis for the new tissue, even in the case of those organs which subsequently exhibit an excess of carbonate of lime. After considering all these facts, we can scarcely entertain a doubt of the positive influence which the phosphates exert on the formation of the tissues and organs. The effects and counteractions reciprocally induced by the phosphates and organic matters in the development of the tissues and in their maintenance, are subjects which still require elucidation. If any doubt still exist as to the share taken by the phosphates in the formation and functions of certain tissues, the observation made by Liebig, must we think, finally set them at rest; we refer to the fact noticed by that observer, that herbivorous animals take up a very small quantity of phosphates in their food, and although their blood is very poor in those substances, their tissues and organs contain as large a proportion of these salts as the corresponding parts of the carnivora. The phosphates must, therefore, be especially attracted and retained by the tissues in the organism of the herbivora, in order that they may there fulfil definite effects corresponding to the objects of the several organs, which could not be fulfilled by the other substances which are supplied in abundant quantities in the vegetable food of these animals. The very variable amount of these salts which we meet with in the blood of herbivorous as well as carnivorous animals, and which obviously depends only upon the nature of the food, or, in other words, upon the quantity of phosphoric acid which it contains, led Liebig to adopt the view that the phosphates do not exert any perceptible influence upon the process of the formation or the main functions of the blood, that is to say, upon nutrition and the development of heat. The facts we have already considered, and those which still demand our notice, coincide so fully with Liebig's view, that future investigations are not likely to modify it. We shall revert at the proper place to the relations of the phosphates in secretion, excretion, and similar processes.

The *alkali* and the carbonates predominate in the liquor sanguinis (serum + fibrin), in the same manner as the free acid and phosphates in the fluids of the tissues. We have seen that the alkalinity of the liquor sanguinis is not induced by the free alkali, but by certain saline compounds of alkalies, and more especially of *soda* with albuminous substances on the one hand, and with carbonic acid, and in part also with phosphoric acid, on the other hand. The albumen of the blood-serum is combined with soda in at least a two-fold proportion, constituting an acid and neutral, or

a neutral and a basic compound, according as we calculate its atomic weight. We have already described, under the head of Albumen (vol. i, p. 334), and under that of Blood (vol. ii. p. 208), the reactions which show that the blood-serum contains two albuminates of soda, one of which is rich and the other poor in alkalies, and that these are mixed together in variable proportions; it is only in diseases that free albumen, held in solution solely by the salts of the serum, can be obtained. This relation even might of itself aid us in conjecturing the effects of the alkali, or in other words, the purpose it accomplishes in the blood. The somewhat lax combination between soda and albumen will always be disposed to give off the alkali, as soon as acids are formed in the blood, or are conveyed to it from other parts of the body. The provision by which the blood is surrounded by acid fluids, and which enables it to expend a portion of its alkali in destroying the acids without by that means losing its alkaline character, is one which demands our fullest consideration; this alkalinity of the liquor sanguinis would, however, very rapidly be destroyed, owing to the abundant supply of acid fluids, and the great tendency of the latter to be converted into alkaline and neutral fluids, if the newly formed salts were not readily and quickly decomposed into carbonates, and in part also were removed unchanged from the blood.

The following seem to be the only considerations which are able to assist us in determining the causes which maintain the alkalinity of the blood at a tolerably constant degree, and the objects which are effected by this constancy. We need not here seek for any complicated modes of explanation, for the question to be determined is simply this: what effect will the alkali necessarily exert on organic bodies under the relations prevailing in the living blood? As far as these relations are known to us, it would appear that the one which especially claims our attention is *the simultaneous presence of oxygen*. The first principles of chemistry teach us that the tendency of oxygen to combine with certain elements is extraordinarily strengthened by the presence of alkalies, but it is scarcely necessary to enter more fully into the chemical laws and experiments which refer to this subject, and which have been already considered in various parts of this work. We will, therefore, limit ourselves to a brief notice of the most important experiments, which show the necessity that the collective organic constituents of the blood should be subjected to a process of gradual oxidation by the simultaneous presence of oxygen and loosely combined alkalies in the blood. The oxidation thus gradually

proceeding extends itself in organic substances, not merely to the disintegration, step by step, of one atom after the other, but also to the individual atoms of their constituents; that is to say, it is not, for instance, one atom of sugar after the other which is directly converted into carbonic acid and water, but whilst the separate atoms of hydrogen of the sugar are oxidised, there are formed various derivatives before we obtain the final results of carbonic acid and water. The length of time which, as Liebig* has shown, is required for the completion of many chemical processes external to, and independent of, the influence of living organisms, makes the gradual and slow course of chemico-vital processes less remarkable than it was formerly supposed to be. In order that we may take our stand on direct observation, we will pass in review the individual constituents of the blood, and briefly consider their relations whilst they are simultaneously subjected to the influence of the free or slightly combined alkalies and of the oxygen at the temperature of the living body.

We will begin with the *organic acids*, which readily and in no inconsiderable quantity transude into the blood. Every one who has spent even a short time in a chemical laboratory is aware of the rapidity with which organic acids, or rather the salts which they form with alkalies, begin to decompose when there is an excess of the alkali, even where there is a very slight access of oxygen. Fluids previously colourless become brown; we generally remark the formation of vegetable growths; and a closer examination shows that products of oxidation, such as succinic acid, &c., are generated. Liebig has even recommended gallic and pyrogallic acids as the best eudiometric agents, owing to the high oxidising capacity exhibited by their alkaline salts. The well-known discovery of Wöhler, which has justly excited so much attention, is, therefore, nothing extraordinary, and certainly does not prove that the animal body possesses an altogether special oxidising capacity, equalling in intensity our strongest oxidising agents. The means are precisely the same by which organic acids are consumed both within and without the organism; the apparent intensity of the oxidising power in the blood is not owing to any special force, but is the mere result of a peculiar complication of circumstances.

We have, moreover, seen that the *carbo-hydrates* contained in nutrient matters for the most part reach the blood in the form of grape-sugar. We can hardly wonder at the rapidity with which

* Ann. d. Ch. u. Pharm. Bd. 65, S. 350-352.

the latter disappears from the circulation, if we remember that this sugar, when associated with an alkali, is capable of taking up combined oxygen, and of withdrawing it from oxide of copper and many other oxides.

Our experiments show that a less striking influence is exerted by the alkalies on the oxidation of the *fats* and *fatty acids*; indeed, direct observations appear to show that the fats in the blood are oxidized much less rapidly than the carbo-hydrates, or even than the albuminous substances. Urea may be detected in urine as a product of the oxidation of the nitrogenous matters of the food, long before the combustion of the fats can be recognised in the augmentation of the expired carbonic acid (see Nutrition); whilst facts may be advanced in proof of the gradual oxidation experienced by the fats under the action of an alkali and oxygen. We need only refer to the occurrence in the blood of acids homologous to the solid fatty acids, as for instance, in certain secretions, and more especially in the sweat, where the whole series of acids, from formic to caproic acid, has been exhibited with tolerable certainty. Thus, too, butyric fermentation, like lactic fermentation, requires the addition of equivalent quantities of the alkalies for its perfect accomplishment. Although we may deny the appellation of fats to those lipoïds, such as cholesterin and serolin, which most probably are formed only in the blood, they betray in many of their properties so near an affinity with these bodies, that in our ignorance of their origin, it would scarcely seem at variance with the truth, were we to refer them to the oxidation of the fats as residua poor in oxygen, in the same manner as we refer humus to the decomposition of wood.

Chevreul and Scherer have recently shown that *hæmatin* (the colouring matter of the blood) when dissolved in alkalies is able to continue unchanged for a prolonged period, and that on the access of atmospheric air it instantly attracts oxygen, and becomes converted into a colourless body. The want of a more careful examination of these facts has hitherto prevented the exact comparison of this form of metamorphosis with that which occurs in the blood.

No one can doubt that the *albuminous substances* of the blood undergo a gradual oxidation before they can be employed in the formation or renovation of the tissues, although we certainly are still unable to determine the extent to which the alkalies influence their oxidation and further metamorphosis. We know only this much, that the alkali of the blood must aid in abstracting and

oxidising the sulphur which is peculiar to all protein-bodies; and we need only refer to the method recommended by Mulder for the exhibition of the albumen-protein and the fibrin-protein, to show the importance of the alkali in this form of metamorphosis. Hitherto, at least, we have not arrived at any proof of the co-operation of the alkali in the further oxidation of the albuminates.

It certainly would seem probable, from a careful examination of the chemical facts in our possession, that this simultaneous action of the alkali and of the free or imperfectly fixed oxygen upon readily oxidisable substances, might afford an explanation of the entire process of oxidation in the animal organism. But this is by no means the case, and the present affords an instance of the danger of being led astray, by perfectly correct but isolated facts, to adopt extreme and exclusive conclusions. The highly complex chemical processes which prevail in the lower sphere of vitality, are not of a kind to be comprehended in their entire complication of actions and reactions, by one individual function taken indiscriminately from amid the involved and inseparable links of the great chain of causes and effects; for even when, by the strictest application of the inductive method, we have thoroughly investigated the most important factor of a process, we have by no means elucidated the process in all its bearings. We frequently enough encounter contradictory phenomena, which sufficiently show that we are deficient in the elements necessary for tracing the whole of these phenomena in their causal connection. Such is the case here. If, for example, we were to draw the conclusion from these facts, that the process of oxidation could not be accomplished in the animal organism without the concurrence of free oxygen and an alkali, we should err quite as much as if we were to conclude from the same premises that all oxidisable matters which have once reached the blood must be consumed, provided only there were enough oxygen and alkali present for their oxidation. The following examples will serve to show the erroneousness of such a deduction. Starting from the proposition above referred to, the opinion has been advanced that diabetes mellitus depends solely on the absence of the necessary quantity of alkali in the blood in this disease, and that consequently the sugar is no longer consumed in the blood (Mialhe). So far as my direct investigations of the blood of diabetic patients extend, the most careful ash-analyses do not show that there is any such diminution of the alkali, nor do the analyses of the serum exhibit any diminution of

the albuminate of soda. But as comparative analyses of this kind are attended with considerable difficulty, and as the concurrent circumstances might possibly invalidate the correctness of this view, we will turn to other investigations connected with this subject. Bernard, who, as we have already stated, injected a solution of grape-sugar into the veins of dogs and rabbits, thought he could perceive that the sugar not only did not pass into the urine, but that the latter secretion was even rendered alkaline. Without including my previous experiments, which led to precisely opposite results, I have very recently injected grape-sugar, prepared from starch, into the jugular veins of 37 rabbits and dogs;* but in no single instance was the previously acid urine rendered alkaline; and in no single case was grape-sugar absent from the urine. Quantitative determinations showed that even 0·1 of a gramme of grape-sugar could be detected in the urine of a rabbit weighing 2,150 grammes. The greater part of this (0·1 of a gramme) of grape-sugar passed into the urine, even when the rabbits had fed before and after its injection on cabbage-leaves, carrots, grass, and other substances rich in alkalies, and the alkaline urine of these animals did not retain its alkaline character, notwithstanding the abundance of alkalies contained in the food, but acquired, in opposition to Bernard's assertion, an acid and often a very intensely acid reaction. Finally, I convinced myself in two cases that rabbits into whose veins very small quantities of starch-sugar had been injected (which might in other cases be detected in the urine) did not void any sugar, provided they had received no succulent food either shortly before or after the experiment, and hence did not require to pass urine. A similar result was observed when urine was artificially discharged by pressure on the region of the bladder. It appears that sugar can only be separated from the blood when there is an excess of water in the latter, for it is only by the prolonged continuance of sugar in the blood that it can be thoroughly consumed; but the urine here is not rendered alkaline, but strongly acid, as is always the case with fasting rabbits. The sugar, moreover, passes so rapidly into the urine that it may frequently be detected five minutes after its injection (and that even when only 0·1 of a gramme has been injected). This rapid separation of the sugar from the blood, and its decomposition in this fluid, if from a deficiency of water it be retained sufficiently long, seem to favour the hypothesis that the cause of the appearance of sugar in the urine

* Ber. d. k. sächs. Ges. der Wiss. Jahrg. 1852.

is solely owing to the blood not being sufficiently rich in alkali to aid in the oxidation of the sugar. With a view of determining this point, I injected caustic alkalies or their carbonates, in association with grape-sugar, into the veins of rabbits; but even in these experiments the wholly unexpected result ensued that, notwithstanding the caustic alkalies or their carbonates, the urine not only contained sugar, but also exhibited an acid reaction. More exact and often-repeated experiments on rabbits afforded the following explanation of this remarkable phenomenon. When 1 equivalent of sugar with 1, 2, or 3 equivalents of caustic potash or its carbonate, was injected, or when the sugar and potash-compound artificially prepared from alcoholic solutions was injected in such quantities that 0·1 of a gramme of sugar reached the blood, the urine remained alkaline for at least ten minutes after the injection, becoming then decidedly acid, in which state it continued for at least five hours, even when the animals had been fed in the interval upon green food. In the seventh hour the free acid diminished when food of this kind had been taken; it continued, however, although in a less intense degree, when the animals had been kept fasting. In all cases, however, sugar could be detected in the urine from the first five minutes after the injection to the eighth, and even often to the eighteenth hour. If in these cases the alkali does not act in the manner one might be led to expect from the above hypothesis, the cause is to be ascribed partly to the circumstance that the alkali is removed from the blood more rapidly than the sugar, and partly, and perhaps mainly, to the fact of an acid being formed in the blood (as we see by the constant acid reaction of the urine after the injection of sugar) by which the alkali is saturated, and its action on the sugar thus interfered with. I have unfortunately been unable, from the small amount of material for investigation, to decide what is the acid which is thus produced, but it certainly is neither phosphoric or hippuric acid. We at all events learn this much from these experiments, that no one perfectly correct chemical fact can enable us to foresee and correctly prejudge the result of chemical effects in the living body; and it would, therefore, be no less unsuitable to endeavour to elucidate the mystery of life by rude chemical hypotheses, than it would be senseless to banish chemistry from the sphere of vitality merely on account of some few unsuccessful experiments. The following experiments, which I have instituted in relation to this point, will show the correctness of these views. On gradually injecting very dilute solutions of tartaric and citric acids into the

stomachs of rabbits and dogs (concentrated solutions must necessarily be avoided, as they always induce a morbid condition in the animals), the result to be expected would naturally be, that when the animals had been fed on oats only, or on some food equally poor in alkalies, the normal alkalinity of the blood would be so much diminished that the sugar which had now been conveyed to the blood from the intestine or the liver would not be perfectly oxidised, and would therefore pass into the urine in an undecomposed state. This conjecture has not, however, been verified by my experiments. The urine does not even exhibit any trace of sugar when attempts are made to remove the alkali from the blood by artificial means. Similar but variously modified experiments have also been made by Uhle,* with precisely similar results. It would, of course, be an utterly useless experiment to attempt to gain the same object by injecting acids into the blood.

We must not, however, form too high an opinion of the oxidising force of the blood, however important it may be to the entire animal economy. Thus, for example, we meet with numerous phenomena which indicate the co-existence of a deoxidising process with the process of oxidation; of these we need only instance the formation of substances so rich in sulphur as taurine and cystine, and of others so poor in oxygen as cholesterin, castorin, &c. The most striking illustration of this fact is afforded by the well-known experiment, which has recently been confirmed by one of my pupils, Ranke,† that the animal organism acts upon indigo in the same reducing manner as the hot or cold vat; ordinary indigo blue is converted in the primæ viæ into sub-oxide of isatin, (reduced indigo), and may, when dissolved in an alkaline solution, pass through the blood without being perfectly oxidised; hence it may re-appear in an unoxidised state in the urine. If we observe the urine that is discharged after the administration of a few grammes of indigo, we perceive that the fluid assumes a light blue colour, which becomes gradually more intense if it is shaken for a time in the air, until a blue sediment of pure indigo blue is finally formed. This reduction does not originate in the urine itself, since the alkaline fermentation must be set up in the fluid before it can dissolve indigo. This urine, however, has always an acid reaction. If we had not the most evident proof before us that free oxygen was contained in the blood, an unphysiological chemist might consider himself justified in concluding from these facts, that oxygen can-

* Diss. inaug. med. Lips. 1852, p. 19.

† Journ. f. pr. Chem. Bd. 56, S. 17.

not be contained in the blood either in a free or loosely combined form. We can only assume this much, that the process of oxidation in the blood does not possess any high degree of intensity, and that the manner in which the process is here accomplished is more involved than we should at first sight be disposed to believe.

Although we may not overrate the importance of the alkali in connection with the process of oxidation in the blood, the above experiments might probably lead us to the erroneous conclusion that no oxidation can take place within the organism, independently of alkalies. We call such a view erroneous, for independently of the circumstance, that it cannot be denied that a certain oxidation takes place in many acid fluids as well as in the substance of the organs, there are many points which indicate that other conditions may probably contribute to increase the oxidising capacity existing in the blood. Many of the salts of the organic acids, as for instance, the alkaline lactates, tartrates, and citrates, do not become so rapidly oxidised in the air, even when an excess of alkali is present, as the gallates or pyrogallates; for if solutions of these salts be injected into the blood, they not only become much more rapidly oxidised than would be the case externally to the animal body in the atmosphere, but almost more quickly than if the salts were directly incinerated (see vol. i. p. 97). Other substances again, such as salicin, theïne, &c., are very rapidly oxidised in the blood, whilst they continue for a long time to resist the action of alkalies or oxygen, when exposed to their influence at a temperature of 37° externally to the living organism. The rapidity and readiness with which so many substances are oxidised or changed in the blood cannot be solely referred to the simultaneous presence of a mass of bodies undergoing various metamorphoses, to any peculiar condensation in which the oxygen occurs in the blood, or to any similar relations which control the effects of the alkalies; but they must rather be referred to conditions which we are still unable to deduce from any definite physical or chemical processes, owing to the extremely complicated nature of the chemical changes going on in the blood. We will here only refer, by way of illustration, to that condition of oxygen in which it exhibits, as ozone, a far more energetic force of affinity.

However much we may differ from some of Schönbein's modes of explanation and the conclusions he deduces from his discoveries, the majority of the results which he obtains are indubitable facts, whilst it is almost a necessary deduction from his most recent

observations,* that the oxygen in the blood must undergo a change resembling that which it experiences when retained for some time in intimate contact with phosphorus, oil of turpentine, &c. If we fail to recognise the presence of ozonised oxygen in the blood by the ordinary tests, as for instance, iodine of potassium with starch, &c., this is obviously no proof of its absence, for in the presence of a large number of oxidisable matters in the blood, it must necessarily disappear almost as quickly as it is formed. The recent investigations in physiology, which seem at length to approximate towards the solution of the mysterious connection between electricity and nervous action, while they hold out a prospect of being able to determine more definitely the phenomena of free electricity in the animal body, render it more than probable, that the oxygen within the living body—if not in the blood, at all events in other parts—passes into this state of special attractive force, and that in this condition it takes part in the vital processes. At all events we feel that Schönbein's admirable discoveries ought not to be disregarded by physiologists, notwithstanding the obscurity which still appertains to the principles from which we must deduce an explanation of these facts.

But whatever difference of opinion may exist as to the more immediate relations in which the inspired oxygen combines in the body with individual substances, every one must admit the correctness of Liebig's ingenious hypothesis, that the alkalies in the blood promote and maintain the combustibility of the respiratory constituents of the food, and that they consequently serve as essential conditions for the maintenance of animal heat. In the absence of a positive proof of this proposition, we should not wholly reject the negative evidence in its favour. We have often alluded to Wöhler's discovery, that organic acids, such as tartaric, citric, and gallic acids, when they had been introduced in a free state into the body, reappeared unchanged in the urine after their passage through the organism, whilst their alkaline salts, under similar relations, are burnt within the body. We cannot surely explain this fact, except by assuming that the presence of the alkali induces, in the one case, the oxidation of the organic acid, whilst in the other case, the free acid, if present in sufficient quantity, suspends the alkalinity of the blood, and consequently also its oxidising capacity, until it is removed from the organism through the kidneys.

A series of experiments were made some years ago in my

* Journ. f. pr. Chem. Bd. 52, S. 135-149 u. Bd. 53, S. 321-331.

laboratory (by R. Buchheim, now of Dorpat, among others) with the view of determining the quantities of alkaline carbonates, tartrates, citrates, &c., which are necessary to destroy the free acid of the urine, and further to ascertain the quantities of free tartaric or citric acid which must be taken at one time to allow of a portion appearing unchanged in the urine; but notwithstanding every attention to the quality and quantity of the food taken during equal intervals of time, the bodily exercise, and other physiological relations, these observations have failed in leading us to any sharply defined numerical results. In experiments of this nature, a number of conditions exert an influence, the determination of which is in part beyond the power or the calculation of the experimentalist. If we could succeed in determining these intricate relations, we should, at all events, have a check upon our calculations regarding the mechanical metamorphosis of matter in the animal body, in as far as the one series of experiments shows the amount of the free acid which is excreted by the kidneys from the body within definite periods of time, whilst the other series might enable us to determine, at least approximately, the quantity of alkali in the blood, and consequently also the amount of blood in the animal body. Although these experiments have not hitherto advanced the science of physiology, they promise to yield more certain results to therapeutics. As far as we are aware, the relations subsisting between acids and alkalies or the salts of the vegetable acids, and the reactions and constitution of the urine and the sweat, have not yet been considered from a physiological point of view. Physiology has not hitherto been sufficiently applied to medicine, whilst the pharmacologist is ever striving to explain the presumed action of the most irrational agents by apparently rational means, and to defend their respective applications.

With the view of forming some estimate of the oxidising capacity of the animal organism, I formerly turned my attention to the study of the metamorphoses which salicin undergoes in its passage through the body; and I formerly inferred from the reaction which the urine exhibits towards the persalts of iron after the use of salicin, as well as from other experiments, that the organism can only so far oxidise saligenin as to lead to the formation of salicylous acid. Städteler was led to conclude from his experiments on the volatile acids of the urine of the herbivora, that phenylic acid passed into the urine, and that the blue colour imparted to the alcoholic and ethereal extracts of urine, induced by the salts of iron after the use of salicin, depends upon phenylic

acid. Ranke,* who commenced under my direction a more minute examination of this subject, has now obtained the undoubted result, that salicylic acid is formed in addition to salicylous acid; he also obtained considerable quantities of phenylic acid by the distillation of the alcoholic extract of such urine with water. I have, however, not convinced myself that this acid is contained preformed in this urine; it may very readily occur here as a product of distillation. Phenylic acid exerts an extremely poisonous action, so that some symptoms of indisposition ought to manifest themselves after the use of salicin, if this acid were formed from salicin; such, however, is not the case. As it might be conjectured that phenylic acid was separated from the kidneys immediately on its formation, I injected the alcoholic extract of this urine into the jugular vein of a rabbit, but the animal exhibited no morbid symptoms whatever.

I may here observe in reference to the decomposition of salicin in the animal organism, that this substance, which, like amygdalin, is decomposed by synaptase, does not behave in the blood in the same manner as amygdalin, which on being injected into the blood is not decomposed, and hence does not produce poisoning by prussic acid; although when salicin is injected, a portion only passes in an unaltered state into the urine, whilst the larger quantity is decomposed in the blood; for after the injection of salicin into the veins, the urine is affected in the same manner as after its introduction by the mouth. Sugar, which, as is well known, is formed in the decomposition of the salicin by synaptase, cannot be recognised in the urine, even when as much as 0·943 of a gramme of salicin has been injected into the blood. Ranke also found saligenin in addition to those acids in the urine, but no saliretin.

The previous observations leave no doubt as to the function of the *alkaline carbonates* in the blood, and we have already treated circumstantially of carbonate of soda in the first volume of the present work (see pp. 436-440); we will, therefore, only observe, that these salts are able to maintain their function as agents in the process of combustion for an infinitely long period; that is to say, an infinite quantity of organic acids and carbo-hydrates may be reduced by one and the same quantity of these salts into carbonic acid and water; for scarcely is an alkaline carbonate decomposed by a substance of this kind, and deprived of its carbonic acid, before it is reconverted into a carbonate by the combustion of the organic substance; hence we are able to explain how the proportionally small quantity of alkaline carbonates which are present in

* Op. cit.

the blood of the carnivora, and which are only very slightly increased or replaced by the food of such animals, should be sufficient to adapt the materials of respiration for oxidation. We shall revert to the alkaline carbonates and phosphates when we enter upon the more special consideration of the processes of nutrition and secretion.

In treating generally of the distribution of *chloride of sodium* in the animal organism (vol. i, pp. 430-436), we drew attention to the well-established fact that the quantity of this salt varies very slightly in most of the animal juices, especially in the blood, and is restricted within tolerably narrow limits for each class of animals, being wholly independent of the nature of the food and of the quantity of this substance taken up with the food (see vol. i, p. 431, and vol. ii, p. 189); we have also found that the quantity of salt in the excretions, and more especially in the urine, corresponds very closely with the quantity in the food, whilst direct experiments have shown that this salt when it is injected into the blood, is rapidly excreted through the salivary glands, the mucous membranes, and the kidneys. We think that these well-established facts give great probability to the idea that this substance is necessary for the animal vital process. Even if we attach little weight to the instinct which leads certain domesticated animals eagerly to lick up the salt placed before them, and induces the natives of certain districts where salt is scarce to barter slaves and gold-dust for this substance, yet certain experiments on the quantity of salt contained in the blood, together with Boussingault's investigations,* sufficiently show that the use of salt with the ordinary food is an indispensable requisite towards the healthy condition of domesticated animals. Boussingault instituted experiments on two lots of oxen (each consisting of three), one of which he fed for a month on food with which salt had been mixed, and the other on fodder containing no salt, and found by accurate weighing that the salt produced no effect upon the formation of the flesh and fat, or on the quantity of milk, but that towards the close of the period of observation the external appearance and activity of the animals which were being fed upon food to which salt had been added were very superior to that of the animals which were fed without salt, for the latter presented a less smooth and shining coat, while their hair was matted and in part fell off; their gait was also heavy, and they exhibited a cold temperament. The utility of common

* Ann. de Chim. et de Phys. 3me Sér. T. 19, pp. 117-125, et T. 22, p. 116; or Compt. rend. T. 25, p. 729.

salt to the animal organism cannot therefore be questioned, and its importance is further shown by the fact, that during fasting, or when there is a deficient supply of nutriment, in diseases, as pneumonia, &c., the separation of common salt by the urine soon ceases, whilst in those cases in which the blood is deficient in this substance, all the chloride of sodium entering the organism from without is retained until the normal amount is restored.

We have now, however, to consider the more difficult question of the manner in which chloride of sodium contributes towards the metamorphosis of animal matter. We have endeavoured to refer the importance of this salt to the peculiar relations which it exhibits towards the albuminous matters of the blood and of the animal body generally; and it seemed to us that its special use may be to dissolve the pure albumen (or serum-casein of Panum),* together with the albuminate of soda, and thus render it amenable to chemical agencies. Liebig has, however, drawn attention to a very important fact connected with this subject. Gluten is dissolved as readily as muscle-fibrin in water containing hydrochloric acid (see page 84), and is precipitated from this solution not only by more hydrochloric acid, but also by the addition of a solution of chloride of sodium of less strength even than 4%. From these and similar experiments we may assume that the amount of common salt in animal fluids exerts a certain influence on the separation as well as the solution of albuminous substances, although we are unable to demonstrate the individual details with any great exactness.

The mode of action of chloride of sodium in the metamorphosis of animal matter was the more difficult to determine, as it was known to the chemists as an extremely indifferent substance, with very little tendency to form further chemical combinations, urea and grape-sugar being almost the only substances with which it combines chemically. These two facts sufficed, however, to lead Liebig to a very ingenious view regarding the function of this substance in the metamorphosis of matter. It is very probable that the union of urea with chloride of sodium may be far more intimate than its ready decomposition by re-crystallization in water would lead one to conjecture. Thus, for instance, urea is only imperfectly separated by nitric acid from a moderately concentrated aqueous solution, if chloride of sodium be present; urea, moreover, occurs associated with chloride of sodium, even in positions where its presence would not be suspected, as for

* Arch. f. pathol. Anat. Bd. 3, S. 251.

instance, in the crystalline lens of the eye, as was observed by Wöhler, and in the sweat, according to the investigations of Schottin and Favre. Liebig's conjectures may therefore be perfectly correct, that the absence of urea as well as of common salt in the muscular juice, and the passage of urea into the circulation, and its excretion by the kidneys, have a close relation with the presence of chloride of sodium in the blood.

Liebig observes, in relation to the combination of grape-sugar with chloride of sodium, that we are instinctively led to add salt to amylaceous food (which during digestion yields much sugar) in far larger proportion than to other food. The saliva and the pancreatic juice, which more especially conduce towards the conversion of starch into grape-sugar, contain a preponderating quantity of chloride of sodium in their solid constituents.

Diabetic urine always contains, in addition to free grape-sugar, the compound of this sugar with common salt, and it frequently happens that this is the only compound which separates in crystals from diabetic urine. It is not, therefore, an irrelevant question to inquire, on the one hand, into the relation of the chloride of sodium to grape-sugar in the digestion of amylaceous substances, and, on the other, into its separation through the kidneys in diabetes.

Slightly based as the assumptions may be, which can be deduced from the chemical affinities of chloride of sodium in reference to the purposes which this substance accomplishes in the animal organism, there are some facts which can only be explained by a decomposition of this salt in the animal body, and which may therefore throw additional light on its utility in the animal economy. The most striking of these facts is the occurrence of free hydrochloric acid in the gastric juice; at all events, it appears from the most recent investigations of C. Schmidt that free hydrochloric acid may be present in this secretion, without lactic acid or lactates. It certainly remains a mystery for the present how this decomposition of the chloride of sodium is effected. Another less obvious, but not the less remarkable fact is, that even in the blood of herbivorous animals, which take up almost solely potash salts in their food, there are in every 4 parts of alkaline carbonate in the blood-serum at least 3 parts of carbonate of soda, and only 1 part of carbonate of potash, whilst in the muscular juice of carnivorous as well as that of herbivorous animals chloride of potassium is almost solely found. This fact, which was discovered and mainly established by Liebig, shows, on the one hand, that the chloride of sodium in the blood must necessarily undergo

an interchange of constituents with the carbonate and phosphate of potash, and, on the other hand, that nature has assigned very different parts in the animal organism to the alkalies, which are otherwise so similar when considered from a chemical point of view. Similar conclusions may be deduced from the experiments made at Giessen on different terrestrial animals, which showed that the bile, notwithstanding a food rich in potash, contains a large amount of soda, which is combined with the biliary acids. The great persistence of this distribution of these two alkalies in the various animal juices precludes the idea that we have here to deal with a phenomenon which is merely incidental. As we have already observed, it still remains for us to discover the properties to which the soda owes its place in the blood-serum and in the bile, and to explain the purposes which are effected by the accumulation of potash in the juice of the muscular and of all the contractile tissues, as well as in the blood-cells, the plastic exudations, the yolk, &c.

The constant presence in the blood of a tolerably uniform amount of chloride of sodium has led Liebig to the ingenious idea that this very constancy exerts an essential influence on the absorbing power of the blood. This assertion of Liebig's that the constant amount of chloride of sodium present in the blood is an essential agent in the organic process of absorption, must be universally admitted as correct by all who have witnessed even a single endosmotic experiment, and who are moreover well aware that the substances which are actually dissolved in the intestinal canal generally present a far less dense fluid than the blood, and that the kidneys possess a property, which has not yet been explained, of immediately carrying off any excess of water that has entered the blood. If we further add the peculiar relation of acids and alkalies first noticed by Jolly and Graham in diffusion and endosmosis (see p. 218), we shall be disposed, with Liebig, to admit that in the animal body are united all the conditions for rendering the circulating system, by means of the blood, a most perfect suction-pump, which performs its duties without stop-cocks or valves, without mechanical pressure, nay, without regular canals or passages for the transmission of the fluids.

In conclusion, we must again refer to the remarks which have been previously made (vol. i, p.434, and vol. iii, p. 136) in reference to the influence of chloride of sodium upon the development of cells in secretions and exudations. Amongst the latter we found that the most plastic were those which contained soluble phos-

phates and potash-salts, together with moderate quantities of chloride of sodium, whilst those exudations which exhibited a tendency to the formation of pus-corpuscles and cancer-cells always contained very large quantities of chloride of sodium in addition to these salts. It was first observed by Heller,* and subsequently by Redtenbacher,† that in pneumonia, a disease in which the exudation is generally transformed into cytoïd corpuscles (grey hepatization), chloride of sodium is constantly retained in the body, and can scarcely, therefore, be detected in the urine. We find, moreover, in mucus (a fluid which consists almost entirely of a humid mass of cells) the animal juice, which contains a far larger quantity of chloride of sodium than any other animal fluid, whilst even in the cellular tissues as well as in the permanent cartilages and the still-unossified bones, we meet with the largest constant amount of chloride of sodium. We also learn from Frerichs‡ that the synovial fluid, which is so rich in cells and epithelium, contains a large amount of chloride of sodium in solution; and Schottin's recent experiments on the constitution of the sweat have unquestionably shown its richness in this salt. When we consider that the scales of the epithelium of the mucous membranes as well as of the epidermis are moistened by a fluid which is more richly charged than any other with chloride of sodium, and when we observe that the greatest amount of this salt is found in the structures which are richest in cells, we shall scarcely be falling into error if we seek to establish a very intimate relation between the presence of this salt and the formation of cells. Now the horny tissues and the hair, which consist to a great extent, or almost wholly, of cells, contain no very large amount of common salt; but this fact does not prove that the presence of this substance is immaterial to their formation; for the cells of the hair and other horny tissues are either atrophied or destroyed, whilst those of the cartilaginous tissues are still fresh, and hence serve to convey chloride of sodium. If the presence of this salt be necessary for the development of the horny tissues, and especially of the hair, we have a simple explanation of the fact observed by Boussingault in his experiments, that the growth of the hair was injuriously affected in those cattle which were fed without any admixture of salt in their fodder.

In respect to the other mineral constituents which occur in

* Arch. f. Chem. u. Mikrosk. Bd. 1, S. 214.

† Wien. Zeitschr. Bd. 6, No. 8.

‡ Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 463-468.

the animal body, we need only refer to what has been stated in reference to this subject in the first volume, since they take a less important part in the more general functions of life.

Now that we are approaching towards the termination of the general considerations of the arrangement of the most important chemical substrata observable in the metamorphosis of matter, we are forcibly reminded of the ancient saying of Aristippus, that the most probable is often untrue, and the most improbable true. If we are correct in forming a low estimate of the amount of our *positive* knowledge, we ought to exercise extreme caution in the selection of the *principles* by which we regulate our judgment regarding the positive results of our observations and experiments. In our application of chemistry to physiology, we must be especially mindful of the fact that most of the fundamental propositions which at the present time have attained to a general recognition in chemistry, by no means possess such a degree of scientific, or rather of logical, exactness as to place them beyond all dispute. We must not forget that chemistry, like medicine and theology, although perhaps in a more limited degree, possesses a dogmatism of its own. How many of the modes of consideration which are now valid in scientific chemistry, are the mere provisional modes of expressions for certain groups of phenomena, whose analogy is obvious, but whose internal connection and relations of causality are alike incomprehensible and unknown! A chemist of the old school would be indignant if any one were to hint at the faintest doubt of the correctness of the hypothesis that chemical combinations can *only* be effected in accordance with definite numerical proportions, or should venture to assert that gradual metamorphoses, which are alike independent of mathematical laws, and perfectly foreign to the ordinary chemical affinities, might run their course in the highest spheres of vitality. Yet every chemist who regards chemistry and physics as inadequate for the science of life, and on that account deems it necessary to call vital forces to his aid, must of necessity admit the cogency of these doubts; for experiments have alike failed to show that albuminous and histogenetic substances generally are constituted in accordance with perfectly definite numerical relations, or that any supervising agent has been appointed to control the economy of the living organism.

We need not, however, encroach upon the sphere of vitality to show the uncertainty and purely dogmatic nature of many of the more general principles of chemistry. Many principles which

have been established, and are highly useful in investigation, are utterly devoid of any theoretical basis; for many methods have been sanctioned by chemical use which would not stand the test of a logical inquiry. Thus, for instance, no one hesitates to employ predisposing affinity as a means of explanation, although this is nothing more than the personification of an obscure idea. Does not affinity in the mass contradict the fundamental idea of chemical affinity? We do not speak of the theory of the organic radicals, for the constant alterations and the uninterrupted modifications to which this theory has been subjected, sufficiently attest the slight degree of stability which it possesses. And has not the most prolific of all new theories, by which chemical science has been enriched to such an extraordinary extent with the most important facts—the theory of the conjugated compounds, notwithstanding the noble experiments and the brilliant discoveries to which it has led—been in turn subjected to every form of modification?

We must therefore never forget, in applying our chemical ideas to the elucidation of vital phenomena, that the basis on which they are reared is far less firmly established than the fundamental propositions of physics. We find that even in physics new observations and discoveries are daily being made, which long continue to excite our wonder before we are able to reduce them to known physical principles. How many futile attempts have been made to explain Leidenfrost's experiments! And are there not many even at the present day who regard with wonder the experiments of Boutigny? Is the doctrine of molecular attractions so well developed in physics as to preclude the possibility of being further called in question? It is only in the present day that we have had a direct proof of the motion of the earth afforded us by Foucault. Yet how far is chemistry behind physics in its fundamental principles! In endeavouring, therefore, to decide questions of physiology in chemical modes of expression, we cannot exercise too great caution in our deductions; for we know but too well that in most cases we are only supporting one hypothesis by means of another, and that truth in chemistry is very often little more than an idea embodied in a systematic form.

When, mindful of our fallibility, we once more review the character of the substances which nature employs to produce the most varied effects in the living organism, and to realise the most multifarious purposes, we are struck here, as everywhere, by the

wonderful simplicity of the means or the forces by which the world of external phenomena is maintained in a state of incomprehensible alternation. There are only three groups of organic substances through which all the vital phenomena are manifested, and even these groups exhibit the most important internal co-relations. May we not conjecture, although we are still unable to prove the fact, that members of the group of fats may be formed, like those of the group of carbo-hydrates, from histogenetic bodies? And do not the members of the individual groups present such uniformity and analogy in their composition, and even in their properties, that the diversity of the processes to which they give rise is perfectly incomprehensible? We are thus obliged to have recourse to isomerism and polymorphism as a prop to our ignorance, and as the means of affording us at least some clue to the manner in which protein-bodies, which appear almost identical, can be exhibited under such numerous modifications of form, and can so variously influence the mechanism of the living organism. There are almost inappreciably small differences in the composition and qualities of the substances which, as far as we know, are most homologous with ethereal bodies, viz., the fatty substances; yet the different fats do not produce the same or even analogous effects in the animal body. The carbo-hydrates, which to a superficial observer might seem to be destined solely to undergo disintegration in the animal body, exhibit the most various metamorphoses and subdivisions before they are fitted to perform their part beneficially in the apparent intricacy of the vital phenomena. Potash and soda, for instance, are substances which the chemist finds it extremely difficult to keep asunder in his systems, and which frequently appear to replace one another in the mineral kingdom; yet they are employed in life to maintain the most strikingly opposite conditions; whilst carbonic acid, the weakest and most volatile of all acids, is occasionally made to perform the same service in the organism as the powerful and solid phosphoric acid.

It might here be asked whether nature has not employed forces peculiar to itself in regulating, with these few means, the internal economy of animal life, while we are admiring the insignificant expenditure of force which is required to convert these changeable bodies from one form to another. When we see how readily the largest quantities of starch or cane-sugar are converted into grape-sugar by almost inappreciable quantities of diastase or

of acids,—when we further bear in mind what slight means suffice to convert oxide of ethyl into methyloxalic acid, or oxide of amyl into valyloxalic acid,—and when, finally, we consider the various modifications which the protein-bodies experience under the action of the ordinary atmospheric influences, causing them even in some cases (as we see in putrefying cheese) to be partially regenerated,—we can scarcely conceive that any special expenditure of force is necessary to move these masses in the manner indicated. Although we must not suppose that isomerism and polymorphism, or even the laws of ordinary chemical affinity, are able to afford a true explanation of these metamorphoses and modifications of known materials, it cannot be doubted that the same forces are employed within the sphere of life as those which act in the external world, and that a very slight increase of intensity is alone necessary to produce the effects which we perceive in life. If, however, the organism requires so slight a development of force to effect these changes in matter, we shall hardly deem it necessary to assume the existence of a special force of great intensity and applicability to effect the ever-marvellous movements of organic matter; but are rather led to the belief that the same simplicity which nature exhibits in the use of material means, is unfolded on a grander scale in the application of her forces.

Digestion.

As in the second volume of this work, we have treated of the different juices which take part in the digestive process, and have attempted to determine the functions which nature has assigned to each of them, it might appear advisable, before reviewing this process as a whole and in a general point of view, to examine more closely the objects of digestion, that is to say, the nutrient matters themselves in their relation to this process; but as we have there assumed that the reader possessed a general knowledge of the subject of nutriment, it will here be our best course to discuss the process itself, before entering upon the digestibility of individual articles of food, and the action of the various digestive agents upon them.

From the earliest period at which it was attempted to apply

chemistry to physiology, and to afford a scientific explanation of the animal processes, it has been believed that the digestive process, sooner than any other, would be more or less elucidated by these means. Every one recollects that the iatro-chemical school based a great part of their philosophy on the facts which they believed that they knew regarding the digestive process. Since then scarcely any department of the physiology of vegetative life has been made the subject of such brilliant scientific labours as the digestive process. It is needless to name the great work of Tiedemann and Gmelin, for even to the present day we constantly find in this rich treasury of admirable observations, fresh motives to new experiments and to new views; witness the numerous meritorious investigations which have been pursued in the Giessen laboratory, on the chemistry of the juices, and of the materials on which they act. The barbarous experimental physiology of the French created new ways and means, in order to penetrate into the obscure mystery of the digestive process. The very names of Blondlot and Cl. Bernard are indelibly associated with the ideas of well-directed vivisections, performed with extraordinary dexterity. Science had scarcely had time to rejoice over the admirable monograph of Frerichs (written under the superintendence of Wagner) when reports reached us of wonderful discoveries emanating from the Dorpat laboratory, and throwing an unexpected light on many points connected with the digestive process.

But if, in such a department as this, where we seem to be dealing with the most direct actions of chemical forces, we are obliged to admit that the results which to-day we appear to have obtained by the most direct experiment and the most positive observation, are to-morrow rendered doubtful by other experiments and other observations, we should, at all events, learn to exercise caution in expressing our opinion even on apparently the most exact observations. Did it not appear to be an established fact that lactic acid is always present in the gastric juice?—and yet, in many cases, C. Schmidt has demonstrated its absence and the presence of free hydrochloric acid; and even at the present time does not Blondlot still retain his earlier view regarding the presence of acid phosphate of lime in this fluid? Who could expect that after Bernard's most recent experiments on the influence of the pneumogastric nerves on gastric digestion, their influence would be disproved, or, at all events, rendered questionable by the most positive experiments? When fat is brought in contact with the pancreatic juice, French observers recognise its immediate disintegration into fatty

acids and glycerine, while Germans can scarcely perceive that the two substances form even an emulsion. To speak candidly, we are unable to find any motive for the action of the bile, or for its effusion into the intestine, from the many conflicting opinions on the subject, all of which, however, have been deduced from observations; and do we even to this day know what actually becomes of the resinous biliary acids in the intestine? Who could have anticipated from our previous knowledge, that an isolated loop of intestine, with its slightly alkaline contents, would be able to digest flesh? and finally, what rich although as yet inexplicable results may we not hope to obtain from Ludwig's continued experiments regarding the influence of the nerves on the secretion of the digestive juices! In short, the intestinal canal always presents itself to us as the scene of a number of highly mysterious processes, and our ideas still range unsatisfied around the as yet unopened portals of this almost impenetrable subject. Hence, if we see even the most acute investigators rapidly passing from one view to another, we must recollect that what we regard as true is in this case always dependent on the stage of development which scientific inquiry has attained at the time.

In the digestive process, as in many other phenomena in the living body, it might seem possible to anticipate the laws according to which these processes, which are still obscure to us, run their course; but we are as little able to draw any conclusions regarding the causal connexion of the phenomena as regarding the primary object of each perceptible action. Hence we must rest satisfied, according to the manner of our forefathers, with a mere representation, when we are unable to apprehend the internal connexion of different phenomena. Thus we have such a representation when, for instance, we compare the digestive canal with its minutest absorbents to the roots of a plant, and then show that the animal carries about and contains within itself the roots or radicles by which it absorbs its proper nourishment, while the plant is firmly rooted in the soil from which it draws its nutriment. The more striking and apparently applicable such a picture may at first sight appear, the more glaringly obvious become the differences on closer investigation, and hence we may perhaps be permitted to devote a few moments to the consideration of the above comparison. If, in the first place, we take into consideration the radicles, which in the higher animals pass into the internal surface of the intestine, we come upon the capillaries, which envelope the whole canal with the most delicate network, and then upon organs which in their

finest ramifications terminate blindly in minute projections of the inner surface of the intestine, and seem to be specially designed for the purpose of absorption: besides these innumerable media for absorbing the soluble substances from the chyme, we likewise find in the intestinal tube certain glandular or capsular organs, which according to recent views are regarded as being connected with absorption rather than with secretion.

At the first glance it might appear inappropriate to begin our consideration of the digestive process with its actual termination, that is to say, with absorption; but independently of the fact that we have already, in the second volume, entered somewhat fully upon many subjects having reference to digestion, in our remarks upon the digestive *juices*, we are the more resolved to commence here with the final result, inasmuch as we can thus better take a general review of the whole process. If by the term digestion we understand that process by virtue of which nutriment is transmitted, in accordance with chemical and physical laws, into the circulating system for the renovation of those portions of the organs which have become effete,—and if we further establish the fact, that by digestion the food is reduced to a soluble state, or generally speaking, to such a condition that it is capable of being absorbed into the mass of the juices of the animal body,—we take the most natural starting-point, not merely for forming an opinion regarding the proximate object of digestion, but likewise for attaining a deeper insight into the different actions and reactions between the food and the digestive juices. For if we only establish the proposition, that the intestinal absorbents possess no specific indwelling property totally different from other physical forces, and that they no more enjoy a distinct elective power than the radicles of plants, it obviously follows that in the various arrangements which occur in the intestinal canal in connexion with the process of absorption, the difference in the agents of absorption must correspond with the different physical and chemical characters of the substance to be absorbed; and this leads us to the idea, that food (whose nutrient power, moreover, has nothing to do with the question of digestion) stands in as close a relation to the organs of absorption as to the solvent and digestive juices. The group of molecules entering into the composition of a substance, whether we consider the point chemically or physically, must regulate its general behaviour in relation to the agents concerned in digestion as well as in absorption; and hence the agents concerned in digestion, that is to say, the juices effused into the intestinal canal and

the organs of absorption, must necessarily stand in a far closer relation to one another than has generally been supposed to be the case. If, for instance, we attempt to classify the articles of food according to the manner in which they are absorbed in the intestinal canal, such an arrangement must coincide pretty closely with the changes which the different articles of diet undergo through the different digestive fluids. Hence it would be by no means an irrational proceeding, if we divided the different articles of food, first, into such as are introduced in a state of solution into the intestinal canal, and consequently are at once diffused and distributed generally through the animal juices; secondly, into such as are rendered soluble by the digestive fluids, and in this condition are, like the former, more or less diffusible; and lastly, into such as, either dissolved or undissolved, must be first metamorphosed by certain digestive fluids, and even if soluble, do not undergo a simple diffusion, but are conveyed by some special routes into the blood and the body generally—by routes on which they undergo certain, although perhaps small changes before their entrance into the blood.

If, therefore, we would study the digestive process in the more highly organised animals, and would not merely consider the food in connection with the juices to whose digestive action it is submitted, but also in reference to its passage into the blood, we must especially take into consideration the organs of digestion, and the laws or conditions under which absorption proceeds. If further it would appear that the mechanical arrangements which are exhibited in the organisms of the higher animals for the purpose of aiding the chemical actions of the digestive fluids, and of promoting the transition of the materials prepared for nutrition into the general mass of the juices, do not directly pertain to the department of physiological chemistry, we must not overlook the fact, that on the one hand, no definite limits can as yet be drawn between the actions of affinity and purely mechanical molecular motions, and on the other, that a scientific comprehension of the whole process from a purely chemical point of view would be impossible. If we here recur to the previous comparison between the absorbing organs of the intestinal tract and the roots of the higher plants, it at once follows that it is only a system of organs for resorption that can be compared with the roots of plants, and that even here the similarity is less between their mechanical configuration than between the laws according to which the absorption proceeds. These resorbing organs are the minute capillaries which

run through the whole intestinal canal, almost from its beginning to its termination.

In the root-fibrils of the higher plants, whose leaves, twigs, stems, and coarser roots are, as is well-known, invested by a membrane that possesses only little permeability for liquids, we find no canals or special organs corresponding to our ordinary ideas of absorption, but rows of cells which from the delicacy of their walls are specially adapted to endosmotic actions. It requires no very profound knowledge of vegetable physiology to comprehend that during the life of a plant, and even for some time after its death, the cells of the root-fibrils continue to have the opportunity of absorbing water and aqueous solutions from the moist soil surrounding them, while they continue to be deprived of this fluid by the cells lying immediately superior to them. If we only consider the enormous evaporating surface which plants present in their leaves and their stomata, and how these organs are exposed to relatively higher degrees of temperature and a perpetually varying atmosphere, we shall readily perceive how the juices occurring in the leaves and in their vicinity gradually become concentrated, and how the cells inclosing them must collapse if those in their immediate vicinity do not transfer to them a portion of their water; their own fluid contents thus becoming more concentrated, and a necessity for a continuous transmission of a similar kind downwards to the cells of the root-fibrils being thus established. At certain periods the formation of organic matter from the previously liquid or gaseous nutrient matter of the plant may also, in no slight degree, contribute to the increased concentration of the cell-juices, and may thus react on the absorption through the roots. Finally, if we bear in mind that the cells contain solutions of protein-substances, dextrin, sugar, &c., substances which possess far less diffusibility than the salts which are contained in the moisture of the soil, we are compelled to admit that plants present all the conditions necessary for calling into play the most active endosmotic currents, and that the terminations of the roots are excellently adapted for the most abundant absorption. The admirable experiments of Hales may serve to corroborate the correctness of the view, that it is only mechanical laws which are here in force, although some individual points still require elucidation in respect to the process of absorption through the roots.

We have already taken an opportunity of remarking that the capillaries, which form a network around the intestinal canal, constitute the medium through which a great part of the fluid

portion of the intestinal contents is absorbed. We see that here also the known mechanical laws suffice to explain the absorption by capillaries and veins, and we may readily convince ourselves that the same laws of endosmosis here come in question which guided us in our explanation of the absorbing capacity of the roots of plants. We here refer less to the systems of cells, between whose contents endosmotic currents are established, than to the cylindrically shaped membranes in which a tolerably concentrated fluid is continually moving forward—an arrangement which is far more favourable to endosmotic motion than the rows of minute closed sacs which constitute the vegetable cells. We have already mentioned (see p. 243) that the blood, as compared with the fluid contents of the intestine, is so concentrated a solution that the chief current must be directed from the intestine towards the capillaries, and that this direction must moreover be always maintained in consequence of the intestinal fluid generally containing free acid. While we must admit, from these few experimental propositions on endosmosis, that this mechanism in the intestinal canal exerts a suction or pump-like action, we must moreover take into account that the denser fluid of the capillaries is constantly flowing onwards, whilst the liquor sanguinis, which is attenuated by endosmosis, is replaced by a fresh and denser blood-wave. Kürschner* has demonstrated by an excellent experiment, which easily admits of repetition, the extraordinary manner in which this process favours endosmosis. We must take a cleaned portion of small intestine (that of a rabbit, for instance), and place it in a basin filled with a solution of sulphocyanide of potassium, in such a manner that one end of the intestine hangs over the edge, while, by the aid of a funnel, we gradually pour a moderately dilute solution of perchloride of iron into the other end, so that a current of the solution of the salt of iron continuously runs through the gut lying in the solution of sulphocyanide of potassium. When the two fluids which are separated by the animal membrane are relatively at rest, more of the sulphocyanide of potassium passes into the perchloride of iron than conversely (as may be readily seen by the deeper red colour of the fluid on the side of the perchloride of iron); if, however, the solution of the perchloride of iron only run in a slow current, we observe that the solution of sulphocyanide of potassium is far less coloured, while if it run through the membranous tube in a very rapid

* Handwörterbuch der Physiologie. Bd. 1, S. 64.

stream, we can scarcely observe even a faint red tint in the solution of sulphocyanide of potassium.

If we observe far more favourable conditions in the sources of absorption in the intestine than in the roots of plants, this is mainly owing to the circumstances by whose reaction the continuance of the absorption is controlled. It need hardly be observed that the rapid absorption of aqueous fluid would very soon thin the blood and the whole mass of the juices to such an extent as finally to put a stop to any further endosmotic action. But the animal, and more especially the human body, presents two means for removing the excess of water from the blood; one of these is tolerably analogous with what occurs in vegetables, whilst the other is peculiar to certain of the higher animals, including man. Like the leaves of plants, the lungs, and in part also the skin of animals, present so large an evaporating surface to the atmosphere, that here, as in the leaves, an extraordinary quantity of water is volatilised. According to Lindenau's approximate calculation, the surface of the lungs of an adult man amounts to 2,642 square feet, whilst the surface of the skin cannot be estimated at more than 12 square feet, and even if we assume the area of the much-plaited internal surface of the intestine to measure 24 square feet, the excessive difference between the absorbing and the evaporating surface will be sufficiently manifested to elucidate this admirably contrived mechanism. The evaporating surface is not, however, so readily exposed to the air in animals as in plants; for, even under ordinary circumstances, large portions of the evaporating membranes are so closely approximated and even collapsed together, that they are rendered almost inefficient; for the pure, comparatively dry atmosphere does not come in direct contact with these evaporating surfaces, but in general only a mixture of air considerably impregnated with aqueous vapour. To this we must add, that the ingestion of fluid food is, to a certain extent, a voluntary act in animals, and hence a much larger mass of fluid may readily be conveyed to the intestine than the pulmonary and cutaneous evaporation can remove,—a circumstance which might readily induce a disturbance in the whole mechanism. Finally, we must remember that a large quantity of water is generated in the animal even by its vital processes, which must contribute towards the attenuation of the juices, whilst organic substances are generated in the plant by the decomposition of water, and the juices of the cells are thus rendered more highly concentrated.

Owing to these relations, it may readily and frequently happen that the evaporation is insufficient to counteract the absorption in *the higher animals;* and to meet this condition, we find in these animals a mechanism which we are at present unable to explain, but the purpose of which is to remove, in a fluid condition, the excess of water from the blood. We need scarcely refer here to the part taken by the kidneys in accomplishing this function in the higher animals, although this is absent in birds, which drink only little fluid, whilst they exhale a large quantity of aqueous vapour during rapid evaporation, and in the lower animals, which do not drink, and exist under peculiar relations.

This brief notice of the mechanical relations existing between evaporation and the ingestion of fluids into the animal body, is sufficient to show that by the clearer exposition of several physical laws, with which we are still but imperfectly acquainted, we have made an important advance towards the knowledge of the mechanical effects exhibited in the animal body. The process of absorption appears to be so wonderfully simple in all its details, that we can scarcely comprehend at the first glance why nature has thus superfluously added to the capillaries other and special absorbing vessels, namely, the lacteals. Whilst in a past age the transition of fluids from the intestine to the kidneys was conjectured to take place through "*viæ clandestinæ*," we may now examine the "*viæ apertæ*," through which the liquefied nutrient matter passes into the blood, and which, although not entirely devoid of purpose, appear to us almost superfluous when we remember the power of absorption possessed by the blood-vessels. Our knowledge of this fact should teach us not to overlook those phenomena which we cannot freely deduce from the known propositions of the statics and dynamics of molecular motions, and should remind us that cases very frequently occur in physiological as well as pathological conditions, where the capillaries will appear to be either unsuited or inadequate for the purpose of absorption, when judged by the endosmotic actions with which we have already become acquainted. It too often happens, that when a beautiful physical discovery has been made, it has been hastily applied to all analogous relations in the living organism, without considering that the sum of the existing conditions must give rise to the most various modifications of the newly discovered physical proposition. Thus, for instance, on considering more carefully the process of resorption through the intestinal veins, we are struck by a succession of contradictions, which do not admit of being referred

simply to known endosmotic relations. We shall meet with a considerable number of substances which, although they are extremely soluble, and occur in very dilute solution, are unable to enter directly into the intestinal capillaries, while there are many substances which only reach the blood indirectly through the lacteals. Although such facts as these strike us at the first glance as singular, we must not forget that the relations existing between the dissolved parts of the intestinal contents and the veins of the intestine are less simple than the above description might lead us to infer. These fluids, and the walls of the intestinal capillaries, are separated by at least one dense layer of epithelial cells, which are further surrounded by a more or less dense network of filaments of connective tissue. We are unable at the present time to determine *what* modifications these thick layers of organic matter induce through the results of endosmosis, and consequently also of absorption, but that they do effect such changes has been proved beyond a doubt by numerous experiments on endosmosis, which agree in showing that an endosmotic motion is succeeded by numerous alterations depending upon the thickness of the membrane,its morphological and chemical character, the chemical constitution of the fluids between which the interchange is going on, &c. We know that the difference between animal membranes exerts an essential influence on the endosmotic process, although we are still far from knowing how a mucous membrane, a serous membrane, &c., is able to induce or to modify an endosmotic process. We know, further, that external pressure powerfully influences endosmosis; and Liebig's beautiful investigation affords an example how, in consequence of different pressure, we obtain an opposite result from what the fundamental principles of endosmosis would have led us to expect; but we are not acquainted with any mathematical connection between the amount of the pressure and the velocities of endosmotic motion. The influence exerted by the force of different pressures is of the greatest importance in the process of absorption by the intestinal capillaries, for we need scarcely observe that the pressure to which the blood is exposed in the capillaries must contribute very essentially towards the abundant absorption of matters from the dilute solution of the chyme-constituents. If we know the law of endosmosis, in its simplest expression, we are still totally unable to classify according to simultaneously prevailing conditions and definite general formulæ, the differences of its actions. Notwithstanding the efforts of the most distinguished inquirers, such as Poisson, Magnus, Brücke

Liebig, Jolly, Ludwig, &c., we have no comprehensive theory of endosmosis; yet without such a theory we are as little able to comprehend the causal connection of the complicated endosmotic processes exhibited in the living body, as to deduce *a priori* the result of certain endosmotic effects depending upon definite external circumstances. We cannot hope to establish a theory of endosmosis before the laws of the diffusion of liquid fluids discovered by Graham have been elucidated, and the influence of the different nature of porous intermediate walls upon diffusive fluids, that is to say, the relation between diffusion and endosmosis, together with all the circumstances by which the latter is determined, has been adequately investigated. Not until then will it be possible to prove or refute the co-operation of the vital capacities of the organs during absorption. If, however, we still continuously encounter a number of phenomena in the living body, which seem to be at variance with the endosmotic laws with which we are at present acquainted, and if many interesting experiments (as, for instance, those of Böcker*) still appear to defy explanation by simple molecular motion, this merely proves that we are still deficient in the physical knowledge necessary for the comprehension, in a physical sense, of the causal connection of such phenomena. We are further taught that, in order adequately to comprehend the mechanism of absorption, our first task ought to be that of accurately examining the physical conditions of endosmotic actions, and comparing them with the relations which exist in the living body. A great step forwards in science is, however, always made, when we arrive at a clear conception of the problems which we are especially called upon to solve.

As we cannot discover the slightest logical justification in the still imperfectly elucidated processes of absorption for the assumption of vital forces having the power of directing one substance hither and another thither, or of taking up what is useful and rejecting what is noxious, we are thrown back upon the proposition from which we started, namely, that the capacity of a substance for absorption stands in the same intimate relation to its chemical quality as all its essential qualities do to one another (compare vol. i, p. 404). If the capacity of a substance for absorption be not a mere irrelevant property, those substances which are exposed to similar relations of absorption must generally present very definite analogies with one another; the capacity for absorption does and must always coincide with certain other

* Rhein. Monatsschrift. 1849, S. 754-759.

qualities in the same substances. We will here only refer, by way of example, to a group of properties exhibited by soluble bodies which stand in the most intimate relation to one another for each individual body. It cannot surely be denied that the degree of solubility of a substance stands in a definite relation to the coefficient of condensation occurring during solution; and who, moreover, could venture to question that the diffusibility of a substance must stand in certain relations of dependence to its solubility? and do we not proclaim our belief in the intimate connection between endosmosis and the diffusion of fluid bodies, when we regret that we should hitherto have followed a wrong direction, and studied the more complicated processes of endosmosis before we had attempted, as Graham has now done, to refer the phenomena of diffusion to definite laws? Our knowledge is indeed not yet so far advanced as to enable us sharply to define these conditions and relations of dependence, or the connection existing between these different properties; but, at all events, this much is clearly shown, that all these properties are not merely connected together, but that they are also placed in the most intimate connection or relation with certain fundamental qualities in each individual substance. The undeniable importance which this relation of the integral properties of a substance must exert upon it during its entire passage through the animal body, must serve as our apology for entering somewhat fully into this question. It has generally been customary to understand by the term *solution* simply an uniform distribution of the molecules of the dissolving substance amongst the molecules of the dissolving menstruum; and on this account it has been proposed to apply the term *dissolution** (*Auflösung*) to those cases in which the solution (*Lösung*) is evidently accompanied by simultaneous chemically attracting forces. But, in point of fact, such a distribution of the molecules of a solid body amongst those of a fluid never occurs, as far as our knowledge at present extends, unless we at the same time observe, on comparing the sum of the original volumes of the substances to be mixed with the volume of the mixed body, that the entire volume has been diminished by condensation. The merit of having confirmed this fact appertains to C. Schmidt, who has also determined for many substances the degree of condensation exhibited in their solution in certain

* [I merely use this word for want of a better. We have no two words which bear precisely the same relation to one another as the two German words. —G. E. D.]

quantities of water, that is to say, their coefficients of condensation (see vol. ii, p. 4). Schmidt is therefore disposed to assume the existence of a chemical attraction even in the solution, and a "hydratation" in the case of a solution in water. If we conceive the idea of chemical affinity in the more limited sense which has hitherto generally been attached to it in chemistry, and continues for the most part still to prevail, we do not think that the condensation which is here observed affords any stringent proof of the activity of chemical attraction in simple solution. We may certainly give any wider extension that we please to the idea of chemical affinity, but a narrower and stricter limitation of an idea can never do any injury, and cannot in the present case be without a certain significance. The mere condensation of two bodies when they are mixed, is no argument for their chemical combination; for if we are unwilling to admit that the condensation of gases on the surfaces and in the pores of solid bodies presents a proof against this view, Pettenkofer's admirable investigations on metallic alloys must convince us that, in addition to condensation, a development of light may occur, together with an altered condition of many physical properties, without the occurrence of any true chemical combination. An attraction for the water is manifested when a solid body becomes fluid; an attraction is manifested when a solid body, having thus become fluid, undergoes condensation with the water; forces of attraction are manifested when different substances require different periods of time in order to spread or diffuse themselves through a given volume of water.

It might, therefore, be conceived, that the degree of this attraction, manifested in the solution of a solid body in water, would admit of determination, either by comparing together the quantities of the bodies which are able to absorb a definite quantity of water, that is to say, by determining the degree of solubility; or by the calculation of the coefficients of condensation, using the quantities of the heat that is developed as a controlling check; or that we might ascertain the readiness with which a substance is disposed to diffuse itself during perfect rest through a larger quantity of water. It might be supposed, that as all these three momenta speak in favour of an attraction between solid and fluid bodies, the degree of this attraction might be calculated from the different quantities obtainable by the three methods of investigation, and that one method must control another. Such, however, is not the case. It must be regarded as one of the theoretical deficiencies of chemistry,

that the degree of solubility of substances has not yet admitted of being brought into definite relations to their chemical constitution, or even to any other of their properties. Even the coefficient of condensation cannot be regarded as a standard for the amount of this attraction between water and a solid body; for even in the attraction which regulates the chemical combination, it is of no consequence in reference to the determination of its amount; nor has any definite relation been discovered between the modulus of condensation of these bodies and any one of their integral properties. Even the degree of diffusion of soluble bodies does not readily give the amount of attraction between the solid and the fluid; but its dependence upon weight seems to be very clear from Graham's investigations. Although no definite connection can be established even from these three intimately allied relations between water and soluble bodies, we yet learn from previous observations, that certain relations, which are at all events analogous, may be determined for different well-characterized groups of bodies. These relations, however, acquire so much the higher signification, since they are more especially reflected in the groups of substances which play a considerable part in the animal body, and are thus of great importance in our discrimination of the products of the metamorphosis of matter and of absorption generally. C. Schmidt found that the coefficients for 10 per-cent. solutions of chloride of sodium, grape-sugar, and albumen, were 1·505, 0·766, and 0·420. Graham observed the following proportion for the diffusibility of these three substances in 20 per-cent. solutions, namely, 100, 45·36, 5·24. The analogy is here very great, although we may not be able to recognise any equal proportion in these numbers. Moreover, Graham's provisional investigations show distinctly enough that there is a definite relation between the diffusibility and the specific weight of the diffusing fluid; hence the coefficient of condensation must have a direct relation to the diffusibility; at any rate we cannot at present overlook this relation. Urea here presents itself as an important exception; the coefficient of condensation of its 10 per-cent.-solution was found by Schmidt to be less than in any other substance (=0·160), while its diffusibility is, according to Graham's determination, exactly equal to that of chloride of sodium.

Owing to the generally recognised and very comprehensive relation existing between the capacities for diffusion and transudation, it will not surprise us to find that the endosmotic equivalents, when calculated by Jolly's provisional method, should correspond

tolerably closely with the equivalents of diffusion. The definite attraction towards water, which we see so variously expressed in the above cases by solid *soluble* substances, and the attraction shown in the last-named case of solid insoluble bodies to water, equally lead us into a domain of inquiry, in which we receive no aid whatever from empirical bases; although the long-known, as well as the more recent investigations regarding hygroscopicity by Blücher,* by Schwede,† and by Buchheim,‡ and the provisional results obtained by Brücke, Liebig, and Ludwig, agree in showing that even in this relation between the three important bodies already referred to, the most essential differences are observable in respect to the attraction towards water. No physiologist can doubt that all the relations of solid bodies to water must be involved in the explanation of the phenomena of absorption and of the mechanical and chemical metamorphosis of matter; but even if we admit that absorption is nothing more than a function of these various relations, we are not thereby enabled to explain the process of absorption, for we have not yet succeeded in expressing by a mathematically demonstrable formula any of the different kinds of attraction between water and solid bodies, or of establishing the relations which exist amongst them. For how is any explanation practicable, or, in other words, how can we refer phenomena to laws, when we are ignorant of the laws themselves? We may, however, conclude from the scanty facts before us, that the movements of soluble matters within the living organism, and more especially the phenomena of absorption, must be supposed to depend upon certain physical laws. Thus tremble and fall the last feeble supports of the old and naïve belief in an instinct, or a certain spiritual capacity of the absorbing organs. The time may, however, come, and perhaps is not very remote, when we may include amongst "comprehensible ideas" the properties of every substance whose relation to the animal body may be brought into question; when the zoological department of physiological chemistry will no longer be limited to the enumeration of a few qualities of bodies, either arbitrarily or accidentally selected, but will indicate all without exception—the coefficients of condensation of their solutions as well as their absolute solubility, their diffusibility as well as their volatility, their endosmotic as well as their chemical equivalent, their hygroscopicity as well as their fusibility,

* Pogg. Ann. Bd. 50, S. 541-562.

† De Hygroscopicitate, diss. inaug. Dorp. Livon. 1851.

‡ Arch. f. physiol. Heilk. Bd. 12, S. 217-243.

&c., &c.; and when all these qualities will be elucidated in their most intimate relations to one another. None of these properties should for the time to come be regarded as accidental, for in nature nothing is accidental; the different properties of matter are the necessary result of certain fundamental conditions. When once we shall be able to form a logical judgment of the nature of those substances in which vital phenomena are manifested, when sharply defined ideas of the diversity of matter can aid our judgment regarding the relations of each individual substance to the whole, we may perhaps be able to express, in the simple but clear language of mathematico-physical conception, those conclusions which are deducible from our sensuous observations of the movements of matter in the living body. We shall not on that account be less able to contemplate the wise arrangements of the animal organism, although we may no longer indulge in visionary dreams of the spirituality of matter, or seek to conceal our own inactivity in the incomprehensibility of nature; for these very arrangements are merely the perfected expression of that which may be attained by the co-operation of simple physical forces, when acting upon differently formed and qualified matter under the most various mechanical conditions.

Although such a future may yet be far distant, and the attainment of such aims may require the most arduous efforts of many zealous labourers in science, we yet know the direction in which our endeavours will secure a satisfactory result in this department of our inquiries. We know what we have to seek, and, emancipated from a belief in supernatural forces of matter, we feel that we are not striving for that which is unattainable, but that every step and every scientific result, once gained, will bring us nearer to the goal of our desires.

This being the point of view from which we began our analysis of the movements of matter in the animal organism, it will not appear singular if we commence the consideration of the process of digestion by establishing the qualities of the objects to be digested. The qualities which principally demand our attention are those which involve the different relations of such matters to water; for these essentially control the form and the nature of the absorption which the matters undergo in the intestinal canal. Now as all the properties of a substance stand in the most intimate relations to one another, we scarcely think that we shall be in error if we insist upon the existence of a certain relation between the capacity of a substance for absorption and its other

relations in the alimentary canal, more especially to the so-called digestive juices. Those substances which have already undergone special molecular displacements before their transition into the mass of the juices, must be conveyed by a different channel from that by which unchanged or only slightly modified substances pass into the blood. We must presume that it depends upon certain more or less prominent properties whether a substance passes directly and without change into the blood, or whether it only reaches its destination by indirect channels and after undergoing various changes. It cannot be owing to accident that those substances which undergo no essential alteration in the intestinal canal from the action of the digestive juices, should be especially qualified for direct absorption through the blood-vessels; the one qualification does, and must undoubtedly stand in some definite relation to others, although we do not clearly understand its nature. It is not only their saline character which renders the alkaline salts so easy of resorption; for there are many other salts which are not resorbed by the capillaries, whilst on the other hand, urea, alcohol, and certain poisons, pass with equal or perhaps greater rapidity into the mass of the juices than many of these salts; nor is it the mere solubility of a substance which influences this easy transition; but it is the combination of several qualities depending upon the fundamental relations of each individual substance, which induces the capacity for absorption in the same manner as these fundamental relations also influence the resistance against the action of the digestive fluids. When, therefore, we find some poisons rapidly absorbed in the intestinal canal, while others are not taken up, we should seek for the reason of these facts, not in a certain and definitely limited instinct in the absorbing organs, but in certain definite, although, unfortunately, not perfectly elucidated fundamental relations in these substances. It, therefore, seems most appropriate to divide the objects to be digested into groups, which, instead of being based upon their nutrient power (and this belongs to the theory of dietetics and nutrition), or with regard to their utility or their injuriousness to the living organism, should be arranged according to their digestibility, that is to say, their greater or lesser capacity for being absorbed.

Before we consider those matters individually, whose absorption is solely or principally effected by the capillaries, we must clearly ascertain in what manner a proof can be adduced that a substance does not reach the general mass of the juices through the lymphatics, but passes directly through the capillaries.

After it had been anatomically proved that the lymphatics and lacteals only communicate with the blood-vessels through the thoracic duct, the following experiments were instituted. The lymphatics or the thoracic duct having been tied, a substance was introduced into the intestine or into a loop of gut, which could either be easily detected chemically in the blood, or whose passage into the blood might be recognised by certain phenomena of poisoning. Experiments of this nature were undertaken by Magendie,* Brodie,† Westrumb,‡ Emmert,§ Segalas,|| Mayer,¶ Bischoff,** v. Dusch,†† Kürschner,‡‡ and others, the principal object being to determine as far as possible the capacity of the blood-vessels for resorption. Another method employed to prove the transition of certain substances into the blood without passing into the lymphatics, consisted in examining the blood and the chyle a short time after certain substances had been introduced into the intestinal canal of an animal. It was shown that many of the matters which will subsequently be enumerated, might be found in the blood, but not in the chyle. Experiments of this kind were made by Flandrin,§§ Tiedemann and Gmelin,|||| Mayer,¶¶ and more recently by Bernard;*** the latter observer, moreover, essentially improved this method, by seeking in the blood of the portal vein for substances which had been introduced into the intestinal canal. As the lacteals convey the fluids which they contain with comparative slowness, it must be assumed that those substances which reappear very rapidly in the blood and in the excretions must be resorbed through the intestinal capillaries, and not previously through the lacteals. We may therefore, according to Westrumb, Stehberger, and others, recognise matters which are resorbable through the blood-vessels, by the extreme rapidity

* Précis de Physiologie. T. 2, pp. 203 et 279.

† Philos. Trans. for 1811, p. 178.

‡ Physiol. Untersuchungen über die Einsaugungskraft der Venen. Hannover, 1825; and Meckel's Arch. Bd. 7, S. 525 u. 540.

§ Meckel's Arch. Bd. 1, S. 178.

|| Magendie's Journal de Physiologie. T. 2, p. 117.

¶ Meckel's Arch. Bd. 3, S. 485.

** Zeitsch. f. rat. Med. Bd. 4, S. 62-71, und Bd. 5, S. 293-305.

†† Ibid., Vol. 4, pp. 360-374.

‡‡ Handwörterbuch der Physiologie. Bd. 1, S. 48.

§§ Magendie's Journal de Physiologie. T. 13, p. 65.

|||| Versuche über d. Wege, auf welchen Substanzen aus dem Magen und Darmcanal ins Blut gelangen. Heidelberg, 1820.

¶¶ Op. cit.

*** L'Union méd. T. 3, pp. 445, 457 et 461.

with which they reappear in the urine or in the pulmonary exhalation.

What are the substances which, according to these experiments, may be directly absorbed by the blood-vessels of the stomach and intestine? Among these numerous and, at first sight, very various matters, we meet, in the first place, with certain tolerably soluble salts, which, whether noxious or innoxious to the animal organism, experience no essential changes whilst within it, and do not exhibit any great affinities towards any constituents of the animal body, namely, all the neutral alkaline salts, whose acid shows no peculiar tendency to enter into special combinations with other matters. To this class, therefore, belong the chlorides of sodium and potassium, iodide and bromide of potassium, the alkaline phosphates, sulphates, chlorates, nitrates, borates, and arsenates, yellow prussiate of potash, sulphocyanide of potassium, and the combinations of the alkalies with non-nitrogenous organic acids. A second group of those substances which are especially resorbed by the intestinal capillaries, are the acids, both mineral and organic. A third group consists of alcohol, ether, wood-spirit, and fusel oil (Schlossberger)*. A fourth group contains many volatile oils, including the non-oxygenous as well as the oxygenous and sulphurous oils, as, for instance, camphor, oil of radish, oil of asafœtida, &c.; to these we may probably also add, combustible and natural odoriferous substances, as musk and the constituents of Dippel's animal oil, &c. A fifth group comprises several alkaloids, whether volatile or non-volatile, as, for instance, strychnine, brucine, morphine, theïne, nicotine; and, finally, there remain to be enumerated certain pigments, which cannot be detected in the chyle, although they may be recognised in the urine, as, for instance, the pigment of alkanna, of gamboge, whortleberries, black cherries, rhubarb, logwood, madder, litmus, cochineal, sap-green, and tincture of indigo.

The great diversity of the substances above enumerated would make it appear difficult, if not impossible, to discover in them any common aggregation of properties by which their capacity for absorption through the blood-vessels might be influenced; but certain other matters, which far exceed in solubility many of those already described, do not, as it would appear from direct experiments, show the slightest disposition to enter through the capillaries into the blood, although they are very readily absorbed by the lymphatics, or else, notwithstanding their great solubility,

* Arch. f. physiol. Heilk. Bd. 9, S. 267.

traverse the entire intestinal tract without being resorbed. We shall subsequently become better acquainted with those substances which are exclusively or principally absorbed by the lacteals, whilst in the present place we will simply refer to such extremely soluble matters as gum, turmeric, &c., which are not absorbed from the intestinal canal either by the blood-vessels or the lymphatics. To the last-named substances belong both the curare-veneno (which is probably identical with the woorara) and the poison of serpents. If from this we were to conclude, as has actually been done, that nature in her wisdom has closed the passage of this poison to the blood by both channels, the fact would scarcely impress us very powerfully, when we remembered that all access to the capillaries or the chyle was alike forbidden to the comparatively harmless gum or turmeric as well as to serpents' poison, which could only rarely find its way into the stomach, whilst it opposes no hindrance to the absorption of other poisons which rarely enter wounds but are of common occurrence in the intestine. These considerations, together with the experiments of Boussingault and Bernard (which certainly still require confirmation), according to which an animal membrane that readily permits the endosmotic passage of saline solutions is completely impervious to curarine, emulsin, and diastase, sufficiently show that the law of a physical necessity is here involved. Considering the striking diversity of the above-named materials, we may still hope, notwithstanding our slight knowledge of the laws of diffusion and of endosmosis through membranes, to discover certain properties common to all these matters, on which we may suppose this great capacity for absorption to depend. It is generally admitted that it is only soluble substances which admit of resorption; but the degree of solubility in these substances is so different, that if there were not a number of very soluble bodies which were not capable of resorption, we yet could not ascribe to their solubility alone the capacity which they exhibit of being absorbed by the capillaries. Unfortunately the greater number of these substances have as yet been so imperfectly investigated in reference to their capacity for diffusion and to the endosmotic equivalent which is undoubtedly connected with it, that we are still unable to demonstrate the dependence of their capacity for absorption upon these properties; but the analogy between substances found by Graham to be very diffusible and many of the bodies already referred to, lends the greater probability to our conjecture; for we find that those substances which are very little

disposed to be absorbed through the veins, are precisely those which Graham found relatively little capable of diffusion, as, for instance, albumen, and in part also, sugar.

Considering the near relation in which the volatility of these substances undoubtedly stands to their diffusibility, we can hardly wonder that there should be so many volatile matters in the class of easily resorbable bodies. The third and fourth groups of these transudable substances especially belong to this class; but there is no group in which we more distinctly perceive the dependence of resorbability upon these physical properties than in the second one; for Graham's experiments on diffusion, as well as the numerous endosmotic experiments which have been made with the acids, explain their easy transition into the capillaries. If we could suppose that the diffusibility and similar properties of a substance were alone dependent upon certain fundamental properties pertaining to it, we should find a certain simplicity in the form of composition of most of the above groups. These substances have either a mere binary composition, or, at all events, like the haloid bases and alkaloids, they have, according to the most recent chemical investigations, a very simple constitution, approximating to the binary law; while such soluble matters as do not belong to the above groups, as albumen, emulsin, gum, and even sugar, have hitherto baffled all the efforts of chemists to comprehend their composition in accordance with the ordinary views of chemical affinity or polarity.

Although we have endeavoured in the above remarks to consider from purely physical points of view the absorbing capacity of the capillaries and the capability of certain substances to be absorbed by them, we hope that our feeble attempt will not be so far misconceived as to leave the impression that we would wish to characterise the process operating in the animal body as actually physical in its nature. We are, on the contrary, far from entertaining such an opinion; for the physical facts presented to our notice do not, in our opinion, present sufficiently strong indications to enable us to establish with completeness any such purely mechanical mode of consideration; we will therefore merely repeat, that the simplicity of the physical principles of explanation are better adapted to give a safe direction to our conjectures and further investigations, than if we were credulously to trust to a transcendental mode of reasoning, without the aid of earnest and profound reflection.

In passing from these provisional remarks to the process of

digestion, and the comportment of different substances while subjected to this process, we have nothing to add to the observations already made, excepting to remark that we shall not here have to notice the digestive fluids with which these groups of substances are brought in contact, since these substances pass from the intestinal canal into the mass of the juices in the same unchanged state in which they entered it. The combinations into which some of these substances enter with acids during the process of digestion, can scarcely come within the scope of the present inquiry, since no essential change is produced by their action.

In turning to the consideration of the individual objects of digestion, our attention is in the first place directed to a group of substances which have been distinguished by the irrational name of the *carbo-hydrates*, amongst which are included cellulose, the different kinds of gum, starch, inulin, lichenin, and the different kinds of sugar.

It must be observed, in reference to *cellulose* or the substance of the vegetable cell, that it belongs to those substances which resist all the digestive fluids and other solvents; and, on account of this property, all those vegetable substances which essentially consist of this substance re-appear unchanged in the excrements of herbivorous and omnivorous animals. It must, however, be borne in mind that this substance (which Mitscherlich,* in his more recent experiments, found to be perfectly isomeric with starch and is represented by the formula $C_{12} H_{10} O_{10}$, although its composition had been previously assumed by Mulder to be $C_{24} H_{21} O_{21}$) is very frequently found to be incrusted with some other perfectly insoluble substance, such as lignin or suberin. When, as in the case of the Beaver, we find the whole stomach, and more especially the cæcum, plugged, as it were, with fragments of wood and bark, without being able at the same time to detect any easily soluble nutrient substances—as, indeed, E. H. Weber† and myself have frequently observed—we can scarcely avoid adopting the opinion that the digestive juices, at all events, of these animals, are capable of exerting a metamorphic and solvent action upon cellulose. This view of the subject seems also to gain confirmation from a circumstance especially noticed by E. H. Weber,‡ that in the beaver, those organs whose secretions more especially contribute towards the metamorphosis of the

* Ann. d. Ch. u. Pharm. Bd. 75, S. 305–314.

† Ber. d. königl. sächs. Gesellschaft d. Wiss. 1850, S. 192.

‡ Ibid, p. 193.

carbo-hydrates are developed in a remarkable degree; thus, for instance, the salivary glands are exceedingly large in the Beaver, amounting, according to Weber's estimate, to 1-118th of the whole weight of the body, whilst in man, for instance, they do not exceed the 1-895th part of the entire weight. In the same manner the pancreas is remarkably voluminous in the Beaver (Weber found that it measured 18 inches in the case of a tolerably large animal). It seems more doubtful, whether the well-known large gastric gland, which is peculiar to the Beaver, bears a direct relation to the animal's digestion of cellulose. If we should be disposed to ascribe to the secretions of this apparatus, which exert so powerful an action on starch, the property of converting cellulose into dextrin and sugar, it must, at least, be admitted that the chemical relations of cellulose to certain solvent and metamorphic agents are in no respect opposed to this view. It is a well-known fact, which was first observed by Schleiden, and has been admirably elucidated by Mulder, that cellulose, by treatment with the second or third hydrate of sulphuric acid, is converted into a substance very similar to starch, and which is coloured blue under the action of iodine. According to Mulder, syrupy phosphoric acid may, in such cases, be used in place of the sulphuric acid. Notwithstanding the acid nature of the contents of the stomachs of Beavers, and however much this large gastric gland seems to imply that the free acid is destined for the metamorphosis of the cellulose, the acids which occur here are always too much diluted to justify us in ascribing to them such a metamorphic action. At any rate, on an accurate micro-chemical investigation of the fragments of wood, bast, and bark found in the stomach and duodenum of the Beaver, I have never been able to perceive that the addition of iodine induced a blue colouration in the cellulose fibres and cells, although this colour always appeared very beautifully after repeated applications of sulphuric acid. The alkaline juices of the salivary glands, the pancreas, and the cæcal glands, probably exert a stronger influence on the conversion of cellulose into starch, and its further decomposition into sugar, than the acid juices of the stomach. For the admirable experiments of Mitscherlich* show us that even very dilute alkaline solutions act upon cellulose, whilst concentrated solutions act more readily and completely than concentrated acids in converting this substance into starch. Hence we must suppose that the greater part of the cellulose undergoes its

* Op. cit.

metamorphosis and solution in the lower portion of the small intestine and in the large intestine, because the contents of these parts in the Beaver exhibit a strongly alkaline reaction. We must here also notice a conjecture, which has derived some degree of support from another beautiful experiment by Mitscherlich. There exists a peculiar ferment for cellulose which is generated during the putrefaction of potatoes, and destroys the cellulose-cells without attacking the starch. Since, moreover, it is impossible to assume that the conversion of starch into dextrin and sugar by the saliva and pancreatic juice can take place without a special ferment, some probability certainly seems to attach itself to the conjecture that a ferment which can decompose cellulose also exists in these juices of the Beaver, and co-operates simultaneously with the alkali in the digestion of this substance. But although anatomical facts, as well as chemical experiments, speak in favour of the digestibility of cellulose (at least, in the case of the Beaver), we cannot regard the view as perfectly proved until more direct proof of its correctness can be adduced. With a view of elucidating this question, I have frequently made a microscopical and micro-chemical examination of the contents of the small and large intestine of the Beaver, but I have unfortunately never been able to determine with certainty that the cellulose-cells obtained from thence exhibited chemical corrosion, or had been converted into a starch-like substance.

Gum is another carbo-hydrate, concerning whose uses in the animal organism, notwithstanding its solubility, there is still considerable doubt. Although this substance is of such rare occurrence in the ordinary nutrient matters, even of the herbivora, that its co-operation in the process of digestion and its application to the metamorphosis of matter, can be of no great importance, its frequent therapeutical application as a dietetic remedy would entitle it to some degree of notice, even if its peculiar chemical and physiological relations did not demand our attention. In the obscurity which still involves the question regarding the digestion of gum, three possible modes of explanation present themselves; namely, that it is converted into sugar before its resorption; that it is resorbed directly and without alteration; or lastly, that it is not at all resorbed, and is consequently completely eliminated with the solid excrements. The first of these hypotheses is entirely disposed of by the result of our former experiments. We certainly know that gum, like other carbo-hydrates, is converted into grape-sugar after prolonged digestion in the dilute

mineral acids; but all experiments which have hitherto been made to convert gum into sugar, or into any other substance, by means of the digestive fluids, such as natural or artificial gastric juice, mixed saliva, or pancreatic juice, have yielded thoroughly negative results. Frerichs* found that gum remained entirely unchanged when digested as long as 48 hours with saliva and gastric juice, nor was it altered after having remained for 3 hours in the stomach of a dog, both when it was introduced through a fistulous opening and by the mouth. Blondlot† instituted a similar experiment. I found‡ that the gum not only always remained unchanged during lactic acid fermentation, and during the conversion of starch into sugar by diastase, saliva, or pancreatic juice, but also convinced myself, by parallel experiments, that the presence of this body invariably retarded that process. I found, from quantitative determinations, that after the gum had been digested for three or four days in a fermenting or digesting mixture, nearly the original quantity might be again recovered. These experiments, therefore, render it very improbable that even a small portion of the gum is converted into sugar during digestion. If, then, gum be actually subservient to the purposes of animal life, it only remains to be assumed that this body may be resorbed in an unchanged state from the alimentary canal, either by the blood-vessels or the lacteals. Tiedemann and Gmelin§ fed a goose exclusively on gum for sixteen days, when it died; they found in the excrements unchanged gum, which was also present in the acidly reacting contents of the small and large intestines. Boussingault‖ caused a duck to swallow 50 grammes of gum-arabic, and in the course of nine hours 46 grammes were recovered from the excrements. I daily injected into the stomach of an old rabbit, which was otherwise fed on cabbage-leaves, 10 grammes of gum-arabic dissolved in 90 parts of water; the excrements retained their ordinary form and consistence, but gum was easily recognised in them. The daily urine was collected, strongly concentrated, and treated with absolute alcohol, and the undissolved residue was then extracted with cold water. The aqueous solution, even in its most concentrated state, did not give any reaction corresponding to the presence of gum, either when treated with silicate of potash, with

* Handwörterbuch der Physiologie. Bd. 3, Abth. 1, S. 806.

† Traité de la digestion, p. 297.

‡ Simon's Arch. f. Chem. u. Mikrosk. Bd. 1, S. 76-82.

§ Verdauung nach Versuchen. Bd. 2, S. 186.

‖ Ann. de Chim. et de Phys. 3 Sér. T. 18, p. 444.

borax, or with sulphate of iron (Lassaigne).* The animal was killed at the end of three days, four hours after it had taken the last dose of gum (10 grammes at a time), but no trace of gum could be discovered by means of these reagents, either in the very small quantity of chyle that was collected from the thoracic duct, or in the blood after the coagulation of all the coagulable matters and the exhibition of the aqueous extract. We cannot doubt, therefore, that even if this substance admitted of resorption, it must only pass in extremely small quantities, and very slowly, into the mass of the juices; nor can we assume the probability of its rapid conversion in the blood, since all chemical experiments prove that gum is far less easily decomposed than other carbo-hydrates, as, for instance, sugar, which, notwithstanding its ready decomposition, may yet be detected in the blood.

If we are not disposed to believe that the absorbing organs possess the property of resisting the absorption of this extremely soluble substance, the question arises, whether the facts hitherto ascertained from physical experiments on the diffusion or transudation of gum, afford any explanation of the above-named physiological experiments. According to Graham, the diffusibility of gum is only half that of starch-sugar, and four or five times less than that of chloride of sodium, whilst, on the other hand, it is more than four times greater than that of albumen. Jolly found that the endosmotic equivalent of gum was considerably higher than that of sugar. The simplest endosmotic experiments with gum are, however, sufficient to show that animal membranes are not impermeable to that substance. Physical experiments only prove, therefore, that gum penetrates through animal membranes less readily than many other substances; and it only remains to show by further experiments what are the mechanical conditions which cause so small a portion of gum to pass from the intestinal canal into the blood; for the experiments which I have already mentioned do not by any means lead us to the conclusion that positively no gum is absorbed, for silicate of potash, borax, and sulphate of iron are such slightly sensitive reagents, that when applied to a mixture of organic bodies (such as we have here to deal with), they may fail in detecting very considerable quantities of gum. It has also been asserted that turmeric is not resorbed in the intestine; but in my experiments I have detected small quantities of it in the blood of rabbits, which had been made to take daily a concentrated solution of this pigment. It must

* Journ. de Chim. méd. 3 Sér. T. 7, pp. 580-582.

for the present remain undecided whether there is any substance soluble in water, for which the ordinary animal membranes would be absolutely impermeable; for Cl. Bernard's experiment, which appeared to show that the curara poison could not penetrate through an animal bladder, requires to be repeated, whilst Bernard is no doubt in error when he believes that he has convinced himself that emulsin and diastase are incapable of penetrating animal membranes; these bodies, like albumen, undoubtedly, however, possess only a small capacity for penetrating animal membranes. With regard to the curara poison, its chemical qualities have been so imperfectly investigated, that we are not yet justified in assuming anything more than that the reason why it exerts no poisonous actions in the intestinal canal may probably be due either to the fact that it undergoes decomposition in that region, or that it enters into combinations which are innoxious to the animal organism. If, moreover, gum, emulsin, diastase, and curara are in point of fact resorbed in much smaller quantities than we should have expected from endosmotic experiments, we must not regard it as impossible that the physical constitution of the intestinal coats may here exert a special influence; for we know that endosmotic experiments often yield different results, according as the mucous or the serous surface of a membrane be turned to the salt that is to be diffused, and that (for example) membranes of caoutchouc and animal membranes act quite differently from one another in regard to water and alcohol. All such relations as these should be clearly comprehended before we venture to form a definite opinion with respect to the behaviour of gum in the intestinal canal, or to assume the existence of vital forces opposing its absorption. At present, therefore, we know nothing more than that the *Potiones gummosæ,* which are such favourite medicines with the physicians of the rational school, can yield to the animal organism only an extremely small quantity of material, and *that* only of a nature to support the respiratory process; and that their uses—if they are of any use—can be merely negative in acute diseases.

As an object of food *starch* is well known to be the most important of all the carbo-hydrates; we know that it is one of those substances which must undergo a preliminary metamorphosis in order to be resorbed, that it is converted into dextrin and sugar (lactic acid being produced only in a limited degree), and finally, that the saliva and pancreatic juice are the means by which this re-arrangement is effected in the atoms of starch. We have so

fully discussed these points in the second volume, when treating of the functions of the saliva (pp. 30–40) and of the pancreatic juice (p. 120), that very few additional remarks are necessary.

If we briefly review the history of starch within the animal organism, commencing with its introduction into the mouth, we find that in this cavity it is more or less impregnated with saliva according to the intensity of the movements of mastication, its own dryness, and other circumstances. Powerfully as normal saliva occasions the transformation of boiled starch into sugar, its influence on the raw starch during the short time that each morsel remains in the mouth must be extremely slight. In the ruminating animals, on the other hand, where the food is for a long time retained in the paunch, and where from the continuous flow of saliva it is exposed to the prolonged action of this secretion, a great part of the starch contained in the food must certainly be metamorphosed; and the same must be the case in the crop of the bird. In all other animals the greater part of the starch passes unchanged into the stomach, where the further action of the saliva upon it is to a certain degree suspended by the gastric juice, when secreted in sufficient quantity. After a due sojourn in the stomach this substance passes into the duodenum, where it is brought in contact with the powerfully acting pancreatic juice, and the commencement of its metamorphosis ensues. Towards the ileum the pancreatic juice disappears, and in its place we find the intestinal juice, which acts somewhat less energetically in effecting the metamorphosis of the starch. The conversion of the starch into sugar gradually follows; the starch-granules become softened on their surface, and, as they dissolve, become converted into dextrin and sugar. Individual lamellæ become separated from the granules, and undergo more or less disintegration, isolated shreds being often perceptible by the microscope after the application of iodine. The farther the starch passes onwards from the jejunum into the ileum, so much the smaller do the granules appear in consequence of the above-mentioned solution of their surface. The enormous development of the cæcum in herbivorous animals seems to indicate that the amylaceous matters are here again exposed to the action of a ferment which exerts some change upon them : but the experiments which have been hitherto made afford no evidence either in favour of or against the view that the glandular secretions which are there poured forth actually yield such a ferment. We know that the first product of the decomposition of starch, dextrin, is so rapidly converted

into sugar, that we only rarely find it in the intestine, and then merely in small quantities. Since, however, we always find sugar in the intestine in association with starch, it is probable that the dextrin, as such, is, like gum, absorbed only in very small quantities. Although it can scarcely be doubted that a great part of the starch taken with the food passes from the intestine into the blood in the form of sugar, yet we may very readily convince ourselves that a by no means inconsiderable quantity of starch is metamorphosed in the small intestine into lactic acid, and in its lower portions, but especially in the large intestine, into butyric acid, and in these forms is more rapidly absorbed than as sugar.

Inulin is affected by the digestive fluids in precisely the same manner as starch: indeed it may be concluded from the investigations which I have instituted (which, however, were not of an accurate quantitative character), that this substance undergoes even a more rapid metamorphosis than ordinary starch.

We now proceed to the consideration of *sugar*, and especially of *glucose*, which, while it certainly demands our notice in consequence of its frequent occurrence in articles of vegetable diet, is of greater importance from its being, as we have just seen, the most ordinary and normal metamorphic product of that most important non-nitrogenous nutrient matter, starch. The question here at once presents itself,—does true glucose undergo any further changes during the digestion of other substances or when digested alone, or is it resorbed unchanged? And after this question has been answered, the following suggests itself,—by what organs is the glucose absorbed from the intestinal canal?

Many references have been made in the preceding pages to the metamorphosis of glucose into lactic acid, butyric acid, and fat; and hence we should scarcely have occasion to refer more fully to the subject if we had not here to determine, at all events approximately, the magnitude or extent of these metamorphoses. It is commonly assumed that the sugar which is introduced into, or first formed within the intestinal canal is absorbed without further change, and very speedily, by the capillaries,—a view which seems to us very far from being satisfactorily established. That a portion of the sugar before it is resorbed undergoes one or other of these changes is almost generally acknowledged, but no direct investigations have as yet been made regarding the quantity that is thus altered, and it has commonly been regarded as extremely small. The reason why it has been supposed that only a small quantity of

sugar is converted into lactic acid is probably dependent in part on the observed fact that the acid reaction of the intestinal contents is not very great, and in part on the belief that sugar which is so readily soluble and is regarded as highly diffusible (not being found in large quantities even in the small intestine) must be resorbed with extraordinary rapidity. Since, as has been observed, direct observations on the quantity of the lactic acid formed in the intestinal canal are not practicable, we must look around us for other positive facts, which may support either the one or the other view; such, for instance, as, if we could accurately determine it, the proportion of sugar that passes in a definite time into the blood or into the chyle, as its quantity in these fluids might be compared with the quantity of the sugar-yielding carbo-hydrate taken with the food. Although such calculations certainly might be made from the investigations previously in our possession, yet I preferred instituting certain experiments bearing directly on this question.*

The experiments were made on horses, whose food consisted of a mixture of equal parts of boiled and raw potato-starch; this was mixed with about one-twelfth of rye-bran, and formed into balls, of which from 2,000 to 3,000 grammes were daily given to the horses at intervals of two hours. The quantity of starch in the dried balls was determined by the method of Liebig and Horsford. They had, additionally, about 1 kilogramme [nearly 2·2 lbs.] of sugar in the 24 hours. This feeding was continued for three days, and on the last day the amount of starch in the excrements discharged in 24 hours was ascertained by digestion with dilute sulphuric acid, and the subsequent determination of the carbonic acid developed by fermentation. The animals were killed about an hour or an hour and a half after the last feeding, when the intestinal contents were examined, and the chyle as well as the portal blood was submitted to a careful analysis in reference to the quantity of sugar contained in those fluids.

The horse A took in the last 24 hours 1584 grammes of dry starch in balls; as 234 grammes were found in the excrements, the animal had consumed 1350 grammes in 24 hours; consequently 1500 grammes of sugar must have been resorbed [nine parts of starch being converted into ten of glucose or grape-sugar].

The horse B consumed 1235·3 grammes of starch on the third day of the experiment; as 321·5 grammes of starch were found in

* Ber. der k. sächs. Gesellsch. der Wiss. Jahrg. 1850. S. 130.

the excrements, 914·8 grammes of this substance, or 1016·4 grammes of sugar, must have been resorbed.

The horse C took 1871·8 grammes of starch on the last day of the experiment, and 413·2 grammes were found in the excrements; hence 1458·6 grammes of starch, or 1620·6 of sugar, must have been absorbed into the mass of the juices.

Hence in these animals, if the starch was converted solely into sugar, 1382 grammes of sugar were, on an average, formed in 24 hours, and transmitted into the blood-vessels and lacteals. As the animals were fed at short intervals of 2 hours, we may assume that 57·58 grammes passed into the chyle or into the portal blood in 1 hour, and consequently nearly 1 gramme in 1 minute. Now the movement of the fluid is not so rapid either in the lacteals or in the portal vein as to lead to the belief that the absorbed sugar is too quickly removed from the neighbourhood of the intestine, or from the abdomen generally, to admit of this substance being qualitatively, if not quantitatively, determined in one of these fluids.

It has been formerly mentioned that it was only sometimes that I could obtain even traces of sugar in the portal blood of horses, there often being no indication of this substance. If previous observers believed that they had detected sugar in the blood of this vessel, and found that the properties of this fluid generally were different from those which I have described, the reason of these discrepancies is very probably to be sought in the methods of obtaining the portal blood. The proper method of proceeding is not at first to lay open the whole abdomen, and then to make a regular dissection of the portal vein; for the blood of the hepatic veins in this case regurgitates, and a portion of it makes its way into the branches of the portal vein; and as the hepatic blood presents peculiarities in its morphological elements, and contains sugar, the experiment must be more or less marred. We should make only a small opening in the abdominal walls, and reaching the portal vein as speedily as possible, we should tie it at the point where it enters the liver. Even Bernard,* when he collected portal blood in this manner, never found a trace of sugar in it. In procuring the portal blood of the horses in these experiments, I guarded against the above-named source of error, and I never found sugar or even a trace of dextrin in it.

Although I have often previously stated the procedure which I adopt for the recognition of sugar, yet I would here remark, in

* Nouvelle fonction du foie, &c. Paris, 1853, p. 23.

consequence of the importance of the case, that I obtained from one of the horses 69·4, from another 53·3, and from the third 77·2 grammes of portal blood, and that I employed at least two-thirds of it for the determination of the sugar. The following was the method of proceeding:—the blood after being neutralized with dilute acid and treated with four times its quantity of water, was coagulated by heat, the expressed and filtered fluid was evaporated, the residue extracted with spirit of $85\frac{0}{0}$, and the spirituous fluid precipitated by an alcoholic solution of potash. The portion insoluble in water was mixed with a little water, filtered, treated with dilute sulphuric acid, for the purpose of effecting the metamorphosis of any dextrin that might be present, and then examined for sugar.

We feel inclined to regard as incapable of proof these singular facts (it being in direct opposition to the previously received belief, that the sugar passes with facility into the blood of the intestinal veins), and either to doubt the accuracy of the chemical analysis, or to get over the difficulty by assuming that there is an extremely rapid decomposition of the sugar in the blood. With regard to the first objection which might be, and actually has been, brought against this experiment, scarcely a larger quantity of blood is necessary for the quantitative determination of sugar in the normal fluid than was employed for this purpose in the above experiments; but there must in every case be more sugar in the blood of the portal than in that of any other vein, and its existence there could not be altogether overlooked. If we should further assume that the sugar absorbed by the intestinal capillaries is rapidly decomposed before it can reach the trunks of the portal vein, we must produce evidence that the decomposition of sugar proceeds far more rapidly in the blood of the intestinal veins than in any other blood. We have already seen in another place, that glucose, like all other kinds of sugar, when it is injected into a vein, very soon reappears unchanged in the urine; even when very small quantities of glucose are injected, it admits of easy recognition in that fluid. Since it has been maintained that portal blood is rich in alkaline carbonates, we might be led to believe that it was the presence of the alkali which caused a more rapid decomposition of the sugar in the portal than in any other blood. This abundance of alkalies in the portal blood might probably give some support to this view, if it did not happen to be a mere incidental circumstance, that is to say, if it were constantly present in portal blood without reference to the nature of the food which the animal had previously

taken; this, however, is by no means the case. In my latter investigations regarding the composition of the blood in different vessels, I have on several occasions (after feeding the animal abundantly on bran) found the serum of the portal blood even far poorer in salts than the serum obtained from the blood of the arteries or of the *vena cava;* thus, for instance, in one case the serum of the arterial blood contained 0·853%, that of the blood of the *vena cava* 0·887%, and that of the portal vein 0·521% of salts; these numbers calculated in relation to the solid residue of the serum in each case give a similar result; in the solid residue of the serum of arterial blood the salts amount to 8·392%, and in that of the *vena cava* to 8·501%, while in that of the portal vein they only reach 4·895%. Even in this portal blood, which was so poor in salts, not a trace of sugar could be found.

It has been already mentioned (p. 234) that sugar, even when injected with one or two equivalents of alkaline carbonate, still passes into the urine.

Since, therefore, it appears probable that only little sugar is resorbed by the blood-vessels of the intestine, the question suggests itself, whether the sugar is not probably taken up in so much the larger quantity by the lacteals. But my earlier observations, as well as those recently made on the chyle of the above-mentioned three horses, are opposed to this supposition. It has been already mentioned (vol. ii, p. 286) that it was only after the use of highly amylaceous fodder that I could detect small quantities of sugar in the chyle of horses, and in my latest experiments with the three horses I arrived at no result which would favour the view that the sugar is absorbed by the lacteals. If we assume that the average quantity of chyle which is poured into the subclavian vein of the horse in 24 hours amounts to 50 kilogrammes [110·23lbs.], as might be inferred from what has been already stated (see vol. ii, p. 292), then in these cases, when digestion was constantly going on, 37·4 grammes of chyle must have passed through the thoracic duct in one minute. The quantities of chyle which I obtained from the thoracic duct in the horses A, B, and C, was 22·567, 18·184, and 25·616 grammes respectively. Now, according to our calculations, we see that about 1 gramme of sugar was resorbed by each horse in 1 minute. If, therefore, the sugar has neither been taken up by the blood-vessels, nor has been previously metamorphosed in the intestine, there must be about 1 gramme of sugar in 37·4 grammes of chyle; but if only 0·1 of a gramme of sugar were contained in this quantity of chyle, it would readily

be detected if we had from 18 to 25 grammes of the fluid for the purpose of analysis. In the chyle of the horse A only 0·029% of sugar was found, and in that of the horses B and C even less. The quantity of sugar passing into the lacteals is consequently very inconsiderable.

Do we then find in the intestinal canal itself any proof that the absorption of sugar takes place so rapidly as is commonly believed to be the case? Direct experiments, which I have instituted with the view of determining this point, do not by any means support the above view. From 1 to 2 grammes of sugar obtained from starch (dissolved in 5, 10, 15, and 30 parts of water) were injected into the stomachs of rabbits weighing from 1·5 to 2·5 kilogrammes [from 3·3 to 5·5 lbs.], and the animals (which had been allowed to take solid food both immediately before and after the injection) were respectively killed half an hour, 1 hour, and 2 hours afterwards. Sugar could always be still found in the stomach, the duodenum, and the jejunum; in the animal that was killed after one hour, sugar was still found in the lowermost part of the ileum; if the animal were killed in 1 hour after taking 2 grammes of sugar, this substance was found in no inconsiderable quantity in the cæcum. The contents of the duodenum and jejunum, which were generally tolerably fluid and even limpid, had a very strong acid reaction, which was less strongly manifested, but was still very distinct in the contents of the ileum. The contents of the cæcum always presented a very strong acid reaction. Further, if rabbits were fed for several days solely with red beet, or solely with carrots, sugar (namely glucose) was found not only in the stomach but also in the duodenum in very considerable quantities; in the jejunum the quantity of sugar that could be detected was smaller, and at the lower part of the ileum this substance had entirely disappeared. The contents of the stomach exhibited a strong acid reaction, and those of the duodenum were rather less decidedly acid; on the other hand, the contents of the jejunum reddened litmus paper very intensely, while those of the ileum were less acid, although stronger than those of the cæcum.

These observations, which were formerly made by myself on cats, horses, and rabbits, have recently been confirmed by numerous investigations conducted in my laboratory, partly by Uhle* and partly by von Becker.†

It needs no circumstantial numerical proof, which indeed could

* Diss. inaug. Lips. 1852.

† Zeitschr. f. wiss. Zoologie. 1853, Bd. 5, S. 123.

never be decisive with such uncertain grounds of support, to show that the gastric juice cannot be the cause of this acid reaction; on this point we would rather trust to the evidence afforded by well-known experiments, which show that even after a flesh diet, which gives an additional quantity of free acid to the gastric juice, the acid reaction often entirely disappears in the jejunum. Putting aside altogether my own observations and experiments, I would here refer exclusively to the very admirable investigations of Bidder and Schmidt* on this subject. After the common biliary and the pancreatic duct had been tied in a young dog, an intestinal fistula was formed, which on the subsequent dissection of the animal was found to communicate with the end of the upper third of the small intestine. A week after the operation, when the wound might be regarded as healed, and all general irritation seemed to have subsided, the following experiments were instituted on the animal:—After feeding the dog with flesh, a greyish white mass, with a strongly alkaline reaction, issued from the fistula; in this case, therefore, the free acid of the gastric juice and that of the flesh itself was not only neutralised, but so much intestinal juice was secreted that the alkalinity preponderated. In this case the alkalinity cannot be referred to a formation of ammonia consequent on putrefaction, which might perhaps have ensued from the suspension of the flow of the bile; for when the bile and pancreatic juice are allowed free access to the intestine, we likewise find the chyme in the jejunum and ileum equally alkaline. This much, however, may be inferred from the above experiment, that the free acid which we observe in the whole of the small intestine during a vegetable non-acid diet, or after the use of sugar, does not depend upon the gastric juice, but must have its source in the food itself.

If the fact be confirmed that a portion of the starch and sugar in the intestinal canal be converted into acid, we have then to ascertain what substance, or what constituent of the intestinal contents it is which induces this change. We have seen that when the saliva, gastric juice, pancreatic fluid, and bile are totally excluded, the intestinal juice itself is able to effect the metamorphosis of starch into sugar, and of the latter into lactic acid. Moreover, starch was observed by C. Schmidt to be completely changed by the intestinal juice into sugar in 30 minutes, and into lactic acid in 5 or 6 hours. While we do not mean to deny that gastric juice (Bouchardat and Sandras), bile (van den Broek) or other fluids that make their way into the stomach, or, indeed, that

* Verdauungssäfte und Stoffwechsel. Mitau, 1852, S. 271 u. 281.

even normal mucus, may not possess this property, or, at all events, may not attain it at the temperature of the animal body, this, at all events, is certain, that all these materials collectively do not so rapidly excite the lactic acid fermentation as the special intestinal juice.

I agree with Frerichs and Schmidt that the pure acid gastric juice of dogs, in the state in which we obtain it from gastric fistulæ, does not convert sugar into lactic acid even after several hours' digestion; but if the gastric juice be mixed with much saliva, or if we add to it a small piece of the glandular coat of the stomach of the pig, lactic acid may certainly be detected in the mixture after 3 or 4 hours. Hence we believe that, at all events at the present time, the possibility of a formation of lactic acid in the stomach cannot be altogether denied, although it is not at all probable that, under ordinary conditions, any appreciable quantity of starch or sugar undergoes this change.

If we allow saliva to remain in contact with sugar of milk, or even with starch, at a temperature of from 30° to 40°, a little free acid is certainly formed, but so long a time (often from 16 to 32 hours) is required for its development, as almost to exclude the idea that the saliva in any degree contributes to the conversion of the sugar into lactic acid.

Heintz and van den Broek* support the view that the bile contributes in a special manner to the conversion of the sugar into lactic acid, and the well-known observation, that we generally find the contents of the duodenum more intensely acid than those either of the stomach or of the jejunum, favours this view; but, notwithstanding this, I cannot unconditionally adopt this opinion, for altogether independently of the circumstance that, as has been already mentioned, the intestinal juice alone, without the bile, can induce the lactic acid fermentation, and that the intensely acid reaction of the duodenal contents admits very readily of another solution, the action of the bile on sugar is of so slow and gradual a nature, that we cannot regard this function even as a secondary object of the flow of bile into the intestinal canal. Every one who has repeated Meckel's experiment of allowing bile to ferment with sugar, in the same manner that Schiel has done (see vol. i, p. 257, and vol. ii, p. 104), must have convinced himself that it is only very slowly that the acidity is developed in the bile; and this is especially the case when we employ for the experiment bile that has been filtered, or that has been removed with extreme care

* Zeitschr. f. rat. Med. Bd. 8, S. 343.

from the gall-bladder. Bile that has been freed by alcohol from mucus, and from which the alcohol has afterwards been removed by evaporation, may be kept for months without undergoing the lactic acid fermentation; mucus is indispensably requisite in this process of fermentation, and this substance acts independently of the bile, and not more slowly when alone than when associated with that fluid, but a far more prolonged action is necessary than within the intestinal canal. It cannot be supposed that any of the lactic acid which is formed in these fermentation-experiments could be saturated by the alkali of the bile; for the quantity of alkaline carbonate in bile is extremely small, and the acids, soluble in ether, which are liberated by the decomposition of the bile (and amongst which I could never detect lactic acid with certainty after twenty-four hours' fermentation) exhibit a very strong acid reaction. I found that ox-gall containing mucus, to which I added sugar of milk, and which was kept at a temperature varying from 20 to 40°, deposited in the course of two or three months a sediment of crystalline cholic acid (Strecker's cholacic acid); the supernatant fluid contained an alkaline acetate and comparatively little alkaline lactate.

Lassaigne* was the first to observe that the pancreatic juice does not possess the property of effecting the metamorphosis of sugar.

If we introduce a solution of grape-sugar into a tied loop of gut (at about the middle of the small intestine)—an experiment which Funke often attempted at my suggestion—we find that in the course of 2, 3 or 4 hours the solution, even if it was very concentrated, has for the most part disappeared, while the intestine itself is very pale and never inflamed (whereas loops of gut into which solutions of chloride of sodium of moderate concentration have been introduced, often exhibit a strong inflammatory injection); the portion of fluid remaining in the loop never, however, exhibits an acid reaction. At the first glance this experiment appears to be in entire accordance with the view held by van den Broek and Heintz, that it is solely by the influence of the bile that the metamorphosis of the sugar into lactic acid is effected; but if we simultaneously introduce bile and sugar into the loop of gut, there is still, after the lapse of the above-mentioned time, no acid reaction in the remaining fluid; it might therefore be regarded as a fair conclusion, that the intestinal juice is as powerless as the bile in inducing this metamorphosis, and

* Journ. de Chim. méd. 1851. No. 2, pp. 69-71.

further, the view that sugar is partially converted into lactic acid, might be held as thoroughly controverted. But we must not limit ourselves to isolated facts, if we wish to obtain a deeper insight into the phenomena of the living organism; for the fact remains beyond all question, that after the use of sugar an acid reaction forthwith occurs in the whole of the small intestine and in the first half of the large intestine, and that saliva, gastric juice, and the pancreatic fluid exert no metamorphic power on sugar, this power being possessed in a slight degree by bile, and in a high degree by the intestinal juice. It is easy to see why, notwithstanding the presence of intestinal mucus and bile, no acid is observed in the isolated loops of gut; for the lactic acid is no sooner formed than it combines with the alkali of the intestinal juice and is rapidly absorbed; hence it is only seldom that the contents are alkaline, being for the most part neutral. It is still, however, difficult to understand how it is that the chyme, when its passage is not impeded by any loop, so constantly exhibits an acid reaction—a fact, to the discovery of which we have not been led by any special predilection for lactic acid; moreover, Schmidt and Bidder have indeed observed it (without, however, attaching any special value to the observation). If the passage of the food through the intestine be interrupted by a ligature, so much bile collects in a short time above it that the intestine becomes much distended at the spot; but even here, after sugar has been taken by the mouth, we find no free acid. We wait, therefore, for further investigations to elucidate the cause of the interruption in the formation of lactic acid, which occurs when a single ligature is applied to the intestine. Unfortunately we have been unable to include the consideration of the enormously large intestine of the herbivora in this investigation: my discovery, that after sugar has been taken by the mouth, it may after a very short time be detected in the cæcum, and that it is there that the greatest formation of acid occurs, would seem to indicate that this portion of the intestine possesses more active functions than we have been led from former investigations to ascribe to it. Certain experiments by von Becker, which have a bearing in this direction, have yielded the most decisive evidence in favour of this view.

If we regard it as an established fact, that even after the abundant use of amylaceous food, neither dextrin nor sugar can be detected in the portal blood or in the chyle, and that we can for a long time trace the presence of sugar in the intestine, even as far as the cæcum, after sugar itself or saccharine food has been taken, the supposition that starch is not merely changed into sugar in

the intestine, but that it very soon undergoes still further alterations, seems to present a greater probability than the assumption that it is merely on account of its great solubility and diffusibility that it passes with extraordinary rapidity into the mass of the blood. But is the diffusibility of sugar actually so great? Graham's experiments, which were instituted with crystallised and fused cane-sugar as well as with glucose, coincide in this point, that sugar has less than half the diffusibility of chloride of sodium; while 58·7 parts of salt are diffused, only 26·6 parts of sugar are diffused under precisely the same conditions. Moreover, the endosmotic experiments which have been made by Jolly and others entirely correspond with the above results; thus, Jolly found the endosmotic equivalent of sugar to be almost twice as great as that of chloride of sodium, and twenty times greater than that of hydrated sulphuric acid. Hence these physical experiments do not by any means justify us in concluding *à priori* that the resorption of sugar in the intestine is an extraordinarily rapid process.

Amongst the numerous contradictions which we meet with in the consideration of the phenomena connected with the behaviour of sugar in the intestinal canal, it seems to be especially necessary to institute further and more accurate investigations regarding this circumstance. Several series of experiments have been carried on at my suggestion by von Becker* on rabbits, which at all events have thoroughly cleared up some of the points in question. I deemed it necessary to put aside for the time the consideration of starch, cane-sugar, &c., and to employ only that sugar in these experiments which is formed in the animal body from these carbo-hydrates before they undergo resorption. In the consideration of the results of Becker's experiments even this point must not be wholly overlooked; for we have introduced into the intestinal canal and the blood far more sugar than is ever found there during the digestion of the amylacea under normal relations; and from this very circumstance several objections have arisen which affect not only Becker's investigations, but likewise several experiments made by myself or Uhle. In the first place, it was established beyond all doubt, by three series of experiments, that after the introduction of large quantities of grape-sugar into the intestinal canal, this substance passed directly into the blood, where, indeed, it often accumulated in such large quantity as to show itself even in the urine. In the first series, saccharine solutions of various strengths were introduced by the previously

* Zeitschr. f. wiss. Zool. Bd. 5, S. 123.

described methods into tied loops of intestine, when an augmentation of the normal quantity of sugar was constantly found in the blood; in some cases it even rose to 0·6%, and could therefore be detected in the urine (see note to vol. ii, p. 427, in Appendix). The same results were obtained from a second series of experiments on rabbits, in which solutions of sugar were injected through the œsophagus into the stomach. The value of the experiment was often diminished by the circumstance that the abnormal distension of the intestine with an aqueous fluid loaded with sugar induced morbid phenomena and interfered very considerably with the resorption of the sugar. The third method of detecting the direct passage of the sugar into the blood, consisted in allowing the animals a free supply of highly saccharine food. In this case also there was found to be a constant augmentation of the quantity of sugar in the blood; it was, however, only when the animals had been very voracious that any sugar could be observed to have passed into the urine. Thus there can be no doubt that a great part of the sugar taken with the food or formed in the intestine during digestion, passes unchanged into the blood: and hence, although sugar is also formed in the liver, the quantity of this substance in the blood is directly proportional to the quantity of carbo-hydrates that have been taken—a fact which Bernard* has been led to deny, from his determinations of the amount of sugar in the livers of various animals, although his own investigations show that the liver of herbivorous animals and birds always contains more sugar than those of carnivorous animals.

Another question of much importance in relation to the resorption of sugar is, regarding the quantity which an animal of known size or weight can take up in a given time. Boussingault† found, in his experiments on ducks, that one of these birds (the weight not being stated) was able to resorb 5·62 grammes of sugar, or 5·26 grammes (the equivalent quantity) of starch in one hour. Von Becker found, in several experiments in which saccharine solutions were injected at intervals of a quarter of an hour into the stomachs of rabbits, that for every kilogramme's weight of the animal there were about 4·5 grammes of sugar absorbed in the hour. No importance should, however, be attached to this determination, since, as we learn by direct experiments, the quantity of sugar resorbed in a given time is very dependent on the concentration of the saccharine solution in the intestine.

* Nouvelle fonction du foie, p. 48.

† Ann. de Chim. et de Phys. 3 Sér. T. 18, p. 460.

The circumstance that has been just mentioned leads us to a most important question in connexion with the general process of digestion. We have pointed out in the introductory remarks to this section, that very little light has yet been thrown upon the manner in which those substances are resorbed which are known to pass, as products of digestion, into the blood. In order to obtain an insight into this obscure subject, it seemed advisable to commence the investigation with the simplest and least complicated part of the inquiry, namely, with the determination of the laws affecting the resorption of sugar. The following means were employed to determine this point. Solutions of grape-sugar, of various but accurately determined strengths, were introduced into tied loops of gut of different lengths, and the animal being killed after 1, 2, 3, or 4 hours, both the quantity of sugar remaining in the loops of gut and the quantity contained in the blood were determined. The following may be regarded as the most interesting of the results which von Becker obtained from this series of experiments, which amounted to nearly 60 in number: *the quantity of the absorbed sugar is altogether independent of the length of the loop of gut or of the superficial extent of the absorbing surface.* This thoroughly unexpected result was confirmed in all the experiments; the quantity of sugar injected into the loop being the same, the resorption remained the same, however large the portion of intestine over which the solution of sugar was distributed; if, however, a very short loop were taken, the rule would not hold good. Thus, for instance, 8 grammes of a saccharine solution, containing 0·278 of a gramme of sugar in 7·722 grammes of water, were injected into tied loops of intestine in two rabbits of equal size; in one of the animals the cubic contents of the tied gut amounted to 27,720 cubic millemetres [about 1·6 cubic inches], and in the other to only 6,800 cubic millemetres [0·4 of a cubic inch]; and yet, after four hours, only 0·231 of a gramme of sugar was resorbed from the former, while 0·225 of a gramme (or very nearly the same quantity) was taken up from the latter. In several experiments it was actually found that rather more sugar was resorbed from the smaller than from the larger loop.

A second fact which von Becker established by parallel experiments with two rabbits of similar size, was equally unexpected. While there is a general tendency to believe that the resorption of the intestinal contents proceeds with a rapidity and freedom proportional in a certain degree to the dilution of the solutions contained in the intestine, he found that, at all events,

for saccharine solutions, precisely the opposite rule held good; for it appeared that when equally large quantities of fluid were injected, the absorption of the saccharine solution stood in a *direct* ratio to its concentration; that is to say, that the more concentrated the solution is, the larger will be the quantity that is resorbed. Thus, for instance, in several experiments with solutions of sugar, one of which was four times more concentrated than the other, there were four times as much sugar taken up from the former as from the latter, in equal times; or, while in the former case 90·6% of the sugar injected into the intestinal loop disappeared, in the latter case only 80% were resorbed during the same time.

These rules, as well as the previously mentioned fact, that the intestinal loop absorbing the saccharine solution must have a size proportional to the quantity of sugar, while an excess of size in the loop exerts no influence on the absorption, are explained by those experiments of von Becker's, which were instituted with the view of ascertaining the amount of absorption in different intervals of time, when equally large quantities of equally concentrated saccharine solutions were injected. If we lay down a curve representing the amount of the absorption of sugar in the different intervals elapsing between the injection into the gut and the complete emptying of the loop, and based upon the sixteen experiments which were made upon this point, we see at the first glance that the absorption of sugar proceeds most rapidly at first, and afterwards more gradually. Four rabbits of equal size were always used in these experiments, and equal quantities of the same saccharine solution having been injected into equally large loops of gut, the animals were killed in 1, 2, 3, and 4 hours after the injection. (Inflammation was recognisable about 4 hours afterwards, at the places where the ligatures were applied.) Now if we perceive that the most abundant absorption took place at the commencement, that is to say, during the first hour, this is only a confirmation of the above law, according to which the resorption proceeds with a rapidity proportional to the concentration of the solution. If, after the death of the animal, we observe the degree of fulness of the loop, we find that after the first hour it is thoroughly filled and distended with fluid, if the solution that had been injected was tolerably concentrated; the volume of the fluid within the loop must, therefore, have considerably increased by the absorption of water from the blood of the intestinal capillaries. It follows from a careful comparison of the numerical results which have been thus obtained,

that the penetration of the fluid into the cavity of the intestine proceeds with a strength proportional to the concentration of the saccharine solution contained within it; and further, that the absorption of the sugar varies directly with this concentration. If the solution within the cavity of the intestine be very much diluted by the absorption of water, the further absorption of sugar only proceeds slowly. The previously mentioned exceptions to the first of these laws strengthen the evidence in favour of this law; for if a concentrated solution of sugar be introduced into too short a loop, into which the influx of aqueous fluid from without is consequently difficult or impossible, we find even after 4 hours that it is strongly distended, and that very little sugar is absorbed. Thus, for instance, from 8 grammes of a solution containing 0·982 of a gramme of sugar, 0·889 of a gramme (or 90·53%) of sugar was absorbed by the loop containing 30,800 square millemetres of superficial area, while only 0·182 of a gramme (or 18·534%) of sugar was taken up from the loop presenting 11,160 millemetres of surface, after the lapse of 4 hours.

It is sufficiently apparent, even from this simple statement of the positive results of von Becker's labours, that unexpected as at first sight many of the facts appear, they are yet in the most perfect accordance with the laws of endosmosis in so far as they are yet known. For if we only remember, for instance, the method by which Jolly determined his endosmotic equivalents, in which, in the place of the dissolved salt, a definite and corresponding quantity of water always enters into the endosmometer, and where 1 part by weight of sugar is always replaced by 7 parts of water, we can at once understand the augmentation in the contents of the loop, which we perceive during the first hour after the injection of a concentrated solution, while the absorption of sugar is going on most actively. If the loop be too short for the concentrated saccharine solution, it can only take up a small quantity of water, and hence only a small quantity of sugar, corresponding to the absorbed water, can be given off; and we thus have an explanation why we observe only a very slight absorption of sugar, associated with considerable distention of the loop, in such cases. Finally, we see from this endosmotic law, why the size of the loop (unless when it be too small) exerts no influence on the absorption of sugar; for if the loop be sufficiently great to allow the equivalent quantity of water to enter, no more sugar than the quantity corresponding to this water can ever escape, however great the loop may be. Since the quantity of water which enters is dependent upon the amount

of sugar in the injected solution, the absorption will be precisely the same in loops of the most varied size, provided the concentration of the solutions be the same.

These few indications are sufficient to show that the recognised laws of physics are perfectly sufficient for the explanation of the resorption of sugar in the intestine, and that we are not justified, from the facts in our possession, in referring intestinal absorption to special vital forces. Hence von Becker's persevering labours have advanced us a further step in the knowledge of the physical phenomena in animal life.

Before we proceed to consider the relations of the fat conveyed from without into the intestine in the process of digestion, we must briefly direct attention to certain carbo-hydrates and non-nitrogenous bodies which have not yet been mentioned. To begin with *cane-sugar*, Frerichs maintains, in opposition to Bouchardat and Sandras, that this sugar is not converted into any other form of sugar (as, for instance, glucose), either by the saliva or the gastric juice. My own observations do not lead me to accord with Frerichs' view. It was only recently that I found in repeated experiments, that after rabbits had been fed with beet-root, glucose was invariably present in the stomach and duodenum, while cane-sugar was never found; even when large quantities of cane-sugar were dissolved in water and injected into the stomachs of rabbits, glucose was the only kind of sugar that could be found an hour afterwards in the stomach and in the whole of the small intestine. Perfectly similar results have likewise been obtained by von Becker in the numerous experiments which he instituted on this subject; it was only rarely that he could trace cane-sugar so far as to the middle of the jejunum, even in those cases in which large quantities of this substance had been introduced into the stomachs of animals (cats and rabbits). Since neither the saliva nor the gastric juice is able to effect a rapid conversion of cane-sugar into grape-sugar (or glucose), it only remains for us to assume with von Becker, than this transformation of cane-sugar into glucose is produced by the action of the substances in a state of change which are always present in the intestine.

Sugar of milk appears, both from my own experiments and from those of von Becker, to comport itself in the intestinal canal in precisely the same manner as glucose; it distributes itself very rapidly throughout the whole of the small intestine, and in about an hour after it has been swallowed may be traced as far as the cæcum; but like glucose and cane-sugar, it occasions an intensely

acid reaction in the jejunum and ileum, which remains for three or four hours after the injection of the sugar.

Vegetable mucus (*Bassorin*) was made the subject of several experiments by Frerichs,* who found that during the process of digestion, at all events the greater part of it was not altered, and reappeared unchanged with the excrements. [Gum tragacanth, in which bassorin exists abundantly, was the substance actually experimented upon by Frerichs.—G. E. D.]

Like Blondlot, Frerichs convinced himself that *vegetable jelly* (*pectin*, and its derivatives) is totally unaffected by the digestive fluids.

No group of nutrient matters has presented so many difficulties to physiologists as that of the *fats*, and even in the present day we must not flatter ourselves that we perfectly understand the process of their digestion.

We shall, in the first place, notice the successive changes which may be perceived to take place in the fat in its passage from the mouth downwards in the different parts of the intestinal tract. We could scarcely expect to observe any changes in the fat while in the mouth and in the stomach; for we have already seen that both the saliva and the gastric juice are devoid of any influence either of a mechanical or chemical nature upon it; and in point of fact, we find on examining the contents of the stomach after the use of fat (whether it has been taken alone or in conjunction with other substances), that the fat itself has not undergone the slightest change. Every physiologist, moreover, coincides in this point, that the digestion of fat commences in the duodenum.

In the duodenum, and still more in its further course along the small intestine, we find that the fat ceases to appear in large drops or semifluid masses; the further we descend in the small intestine, so much the smaller do we find these drops becoming, till at length the fat appears very finely comminuted, and the chyme presents an emulsive appearance. Since we see the lacteals distended with white (fatty) chyle after the use of fatty food, it is obvious that the principal course by which the fat makes its way into the blood is through the lymphatics of the intestinal walls. If, however, we follow this fat, which is easily recognisable with the microscope, in its course from the cavity of the intestine to the finest branches of the lacteals in the villi, we find that notwithstanding repeated rinsings with water, fat-globules may be perceived at intervals on and between them, which, however, only

* Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 807.

adhere externally to the epithelium of the intestinal mucous membrane. The occurrence of these external globules on the epithelium is a perfectly natural phenomenon, and there is no difficulty in distinguishing them from fat-globules within the epithelium and from other cells. Now if we consider the epithelial cells themselves, whether they are still adherent to the villi, or have peeled off in large thimble-like shreds, we very frequently find fat-globules in them, which, however, are not to be observed, or are few in number, after the use of food free from fat. During digestion the cylinder epithelium is often somewhat distorted in form, and presents a distended appearance; the broad margin of the base of the conical cylinder epithelium is raised up into an extremely thin and hyaline, strongly convex, or perfectly hemispherical cover. Below the epithelium we perceive the lacteals commencing in small club-like dilatations, and surrounded by a layer of vesicular or cellular bodies, which appear as if they were imbedded in an undefined fibrous mass, the true parenchyma of the villi; more externally, near the peripheral investment of the villi with cylinder epithelium, there are not only the contractile fibre-cells which were first seen by Brücke, but also the small trunks of the blood-vessels which communicate with one another by a very fine network of capillaries. According to E. H. Weber,* there is, however, a layer of roundish cells, in addition to the blood-vessels and lacteals, between the epithelium and the true parenchyma of the villi; in the fasting state these cells present a collapsed appearance, but during digestion they become filled and much distended. It is, moreover, worthy of remark, that very often (but not always) some few of these vesicles are filled with a dark granular matter, while the great majority, amongst which they are interspersed, are distended with a light fluid exactly resembling oily fat; we very often see a large vesicle (dark in transmitted, but white in incident light), and by its side another vesicle equally distended with a strongly refracting fluid; in addition to the very distended cells of these two kinds, which are for the most part situated on the apices of the villi, we always remark gradual transitions to minute granules, some of which are light and others dark, as far as the immediate neighbourhood of the finest ramifications of the lacteals in the villi. Funke has given accurate delineations of Weber's preparations, in his Atlas (P. 8, F. 1, 2, and 3). While Weber regards these light and dark vesicles as a layer of true cells between the epithelium and the parenchyma of the villus, and is consequently of opinion that the

* Müller's Arch. 1847, S. 399.

epithelium cannot be regarded as in a normal condition without this layer of germs, other investigators, and especially Kölliker,* Bidder and Schmidt,† and Frerichs,‡ look upon these vesicles, as well as the branching lacteals of the villi, only as masses infiltrated into the spongy parenchyma, and consider that these vesicles, whether filled with refracting or granular matters, possess no true walls. Bruch§ adopts this view in a memoir which he has very recently published, and shows that in all probability the branching lacteals running towards the margins of the villi are merely blood-vessels, which are able to resorb fat during the process of digestion equally well with the lymphatics.

As there has hitherto been much uncertainty regarding the morphologico-objective facts connected with the resorption of fat, so also has there been much obscurity and controversy in the views that have been brought forward regarding the mechanical processes by which the transition of the fat from the intestine into the lacteals and blood-vessels is effected; and the reason of this will be readily understood when we take the following points into consideration. The animal body is everywhere permeated by an aqueous fluid; the fats are, however, absolutely insoluble in water and aqueous solutions; hence they cannot undergo diffusion in the ordinary sense of the word, and the irresistible evidence of daily experience demonstrates that oily fluids cannot penetrate through membranes moistened with water. Viewing the case chemically, we may say, that the fats are, in a certain sense, somewhat easily decomposable; but independently of the circumstance that stronger reagents are necessary for this decomposition than we are accustomed to find in the intestine, a closer investigation shows us that the fat found in the lacteals is in precisely the same condition as that which is contained in the chyme, and, consequently, that the assumption that the fat is decomposed during its resorption through the lacteals is inadmissible. We are led, therefore, to the view, that certain special cells in each of the villi are solely devoted to the absorption of fat; the appearance of some transparent vesicles filled with fat, and of other opaque ones distended with granular matter, seeming to confirm this view. The chemist who is in the habit of separating the fats from aqueous fluids, sometimes by a filter saturated with water, and sometimes by one saturated with oil,

* Mikrosk. Anat. Bd. 2, S. 163.

† Op. cit., p. 230.

‡ Handwörterb. d. Physiologie. Bd. 3, Abt. 1, S. 854.

§ Zeitsch. f. wiss. Zool. Bd. 4, S. 282-298.

will probably regard this mode of explanation as satisfactory. Thus, indeed, the absorption of fat in certain superficial parts of the villi could be explained; but not the admixture of fat in their interior, since the fat in the minutest branches of the lacteals is seen to be in a state of extreme comminution, and is mixed with an albuminous fluid. Although the admixture of fat with an aqueous fluid is regarded as impossible upon the surface, yet its possibility is here being assumed where we can no longer make direct observations. All the former attempts to explain the digestion and resorption of fat are open to the same objections, since, as we have already mentioned (in vol. ii, pp. 102 and 115), the property of forming emulsions with oily fat, and, consequently, of promoting the resorption of that substance, has been ascribed by some physiologists to the bile, and by others to the pancreatic juice, although we know that the fatty particles of an emulsion very imperfectly, or scarcely at all, penetrate through a moist filter or a moist membrane. It is, however, impossible to deny that the emulsive condition of the fat essentially facilitates its resorption; the bile may, at all events in association with the pancreatic juice and with the co-operation of the intestinal movements, reduce the fat to a state of emulsion, that is to say, diffuse it in minute particles through the watery fluid; but this in no degree serves to explain the mechanical process of resorption. Since Bidder and Schmidt first proved by their experiments that bile was unquestionably necessary for the digestion of fat (see note to p. 105 of vol. ii, in the Appendix), von Wistinghausen* has succeeded, under their directions, in discovering the physical conditions under which the resorption of fat occurs. He has ascertained that oil cannot be made to penetrate through animal membranes without considerable pressure, but that it may be forced through with comparative facility when the membrane is saturated with a fluid which adheres to, or has an affinity for oil. When the membrane was moistened with a solution of potash, an abundance of saponified oil appeared on this side of the membrane in the course of 10 hours, under the pressure of a column of mercury of from 1·75 to 3·37 millemetres [or from ·068 to ·132 of an inch], and associated with it was free fat which had been mechanically borne along by the soap. When a mixture of equal parts of potash-ley and albumen was employed, the oil passed through the membrane even without pressure, although in very small quantity, while in this case also a soap was formed. The oil, however, passed through animal membranes,

* Diss. inaug. Dorp. Livon. 1851.

without being saponified when they were saturated with such fluids as a solution of soap or bile.

Even if these experiments cannot be considered as having entirely elucidated all the conditions affecting adhesion, they place it beyond a doubt that the presence of bile is essentially necessary for the resorption of fat, since this fluid renders these delicate membranes permeable by the fat. It is, however, obvious, that if the membrane or cell-wall be once saturated with a bilio-oleaginous fluid, it will the more readily permit the passage of more fat, and consequently, that the inequality in the filling of the individual vesicles either with fat or with a granular aqueous fluid admits of a very ready explanation. These differences may, however, manifest themselves more in the outer portion than in the interior of the villi, since the pressure which at intervals is exerted by the organic muscles of the villi on the interior, obviously contributes very much, as von Wistinghausen's experiments show, to the intimate admixture of the oil and the aqueous fluid, which must, therefore, take place at the very commencing points of the lacteals.

If, as we learn from Bidder and Schmidt's experiments, a small fraction of the fat is resorbed, even without the co-operation of the bile, this is to a certain degree explained by the subsequent experiments of von Wistinghausen, even if we are unable specially to indicate the exact pressure or the exact substance which effects the transition of this small quantity of fat.

After the preceding remarks it is obvious that no further proof is required that the fat is principally resorbed by the lacteals. It must, however, be obvious from Schmidt's and my own observations (vol. ii, p. 247), that the capillaries also take up fat, although in less considerable quantities; for the augmentation of fat which we observe in the portal blood of animals a few hours after they have been fed, cannot with any probability be explained by such an assumption as that the carbo-hydrates resorbed by the intestinal capillaries become converted into fat in their passage from the intestinal cavity to the portal vein. The above-mentioned observation of Bruch's, who saw fatty chyle-like masses beside blood-corpuscles in the capillaries of the villi, seems (as there does not appear to be any possibility of error in the observation) to afford the most distinct proof that there is a direct transmission of fat into the blood of the capillaries from the epithelial cells and the parenchyma of the villi.

We now proceed to that group of substances which must undergo an essential change in the intestinal canal before they are

capable of being resorbed ; to this class belong not only the *albuminous substances*, but also their more or less remote derivatives, as for instance, many gelatigenous substances, and likewise a number of less-known matters, as synaptase and diastase, the poison of serpents, curarine, &c. Hitherto attention has naturally been for the most part directed to the behaviour of the albuminous matters in digestion. We have already, when treating of the function of the gastric juice (in vol. ii, pp. 53-60), considered this subject somewhat in detail. We there showed that the albuminous matters are not merely dissolved by the gastric juice, but are likewise converted into matters which, although similar in their elementary composition to the substances from which they were derived, yet differ essentially from them in their physical, and in several of their chemical properties. We have proposed the term *peptones* for the albumen, fibrin, casein, &c., after their metamorphosis by the gastric juice, and we believe that it is these peptones which undergo resorption in order to be again very soon converted in the lymphatics into the well-known coagulable albuminous matters. We have been further taught by the experiments of Bidder and Schmidt, that the gastric juice which is secreted is far from being sufficient for the digestion of the protein-bodies necessary for nutrition (see the notes to the section on "Gastric Juice," in the Appendix), and that the intestinal juice possesses in a high degree the faculty of dissolving the protein-bodies, and thus preparing them for being resorbed (vol. ii, p. 120). This metamorphosis of the protein-bodies, and their subsequent resorption, should, however, be confined solely to the small intestine, which is the only part of the intestinal tract in which true villi occur; for if we had no evidence from comparative anatomy that the cæcum and colon exerted only very little influence on the digestion of the albuminates in carnivorous animals, the direct experiments which have been recently instituted, partly by Steinhäuser and partly by myself, show that albumen and pieces of flesh when introduced into fistulous openings in the lower part of the jejunum, or into an artificial anus, pass off almost entirely unchanged by the rectum (see note to "The Intestinal Juice," in the Appendix).

We shall refer, under this fourth group of digestive objects, almost solely to the protein-bodies and their immediate derivatives; it is, however, not improbable that many other substances which do not possess the high physiological value of the albuminates, may yet comport themselves during digestion in a very similar manner, and we have already mentioned the gelatigenous tissues in con-

nexion with this point. Possibly also we should place in this category certain poisons, which, like the protein-bodies, cannot be directly resorbed by the blood-vessels, but must be first so changed by the gastric and intestinal juices, that after being absorbed by the lacteals they pass as innoxious matters into the blood. Diastase and emulsin are substances which in many points of view are very closely allied to the protein-bodies, although we cannot place them in this class. We know that emulsin undergoes the same changes during digestion as the true protein-bodies; for it has been shown by the experiments of Magendie and Bernard,* that pure amygdalin exerts no injurious effects upon the health or the life of animals, either when swallowed or when directly introduced into the blood; if, however, emulsin be simultaneously introduced into the stomach or into the blood, decomposition is set up in the amygdalin, and the prussic acid which is formed destroys the life of the animal. I allowed rabbits to eat sweet almonds, and injected amygdalin into the jugular vein, 1, 2, 4, and 6 hours after they had fed; the animals remained perfectly vigorous. I then reversed the experiment, and injected emulsin into the vein, while I introduced a solution of amygdalin into the stomach of the animal; symptoms of poisoning by prussic acid very soon presented themselves. Since, however, we cannot demonstrate in this manner that the emulsin has actually been metamorphosed by the digestive fluids, and has consequently lost its influence on the amygdalin, and since it is conceivable that emulsin, like gum, might be incapable of resorption, and passed off unchanged with the excrements, I collected the excrements of a rabbit which had been fed for 48 hours on almonds, and mixed amygdalin with them; but I could detect no trace of any evolution of prussic acid; indeed no decomposition of the amygdalin was induced even by the cæcal contents of the same animal.

A number of other bodies, which have certainly been less accurately investigated, but which coincide in their quantity of nitrogen, in their insolubility in spirit, and in their solubility in water, comport themselves in an analogous manner with emulsin. Of all these substances, *curarine* has probably been most accurately examined, thanks to the labours of Boussingault and Roulin.† This substance, when introduced into the stomach and intestines, does not induce the slightest morbid phenomenon, whilst if it be conveyed into the blood, it causes the almost instantaneous death

* Arch. gén. de Méd. 4 Sér. T. 16, p. 79.

† Ann. de Chim. et de Phys. T. 39, p. 24.

of the animal, without any premonitory symptoms; and very similar, both in a toxicological and in a chemical point of view, is the poison of the viper, as well as those poisons which are produced during contagious diseases, as hydrophobia, glanders, typhus, &c.; this view is, at all events, supported by the recent experiments of Renault,* who convinced himself that both carnivorous and omnivorous animals could, without any detriment, feed upon the flesh of animals which had been affected with these diseases, while the juices of such flesh or similar effluvia, when introduced directly into the blood or into a wound, occasion the most fatal effects.

This peculiar behaviour of all these substances proves that they cannot be resorbed in an unchanged condition either by the capillaries or the lymphatics of the intestinal canal. Since most of them cannot be again recognised in the solid excrements, they must undergo so complete a change through the action of the digestive fluids, that when they at length make their way into the blood, they can no longer exert their former poisonous actions. Even if we cannot altogether agree with Bernard† in his view that animal membranes are absolutely impenetrable to these substances (emulsin, diastase, curarine, and the poison of the viper) this much, at all events, is certain, that these substances, like albumen, exhibit very slight endosmotic force. Mialhe and Pressat‡ have, moreover, recently attempted to show that the fresh albumen of the egg can only penetrate animal membranes when the latter have attained a certain degree of putrefaction; but repeated experiments with various animal membranes (previously treated with alcohol, and afterwards rinsed with water) have convinced me that they are not perfectly impenetrable by albumen, emulsin, and diastase. The only point which is established beyond all doubt is, that all these substances pass with difficulty through animal membranes, and that their diffusibility is extremely small. (Graham found the diffusibility of sugar $8\frac{1}{2}$ times as great, and that of chloride of sodium 19 times as great, as that of albumen). In the preceding remarks we can see the reason why the protein-compounds, which are apparently ready to be applied at once to the purposes of nutrition, must first undergo a metamorphosis through the influence of the digestive juices before they are resorbed. If it were not for the gastric and intestinal juices, soluble

* Compt. rend. T. 33, pp. 532-535.

† L'Union méd. T. 3, pp. 445, 457, et 461.

‡ Compt. rend. T. 33, pp. 450-454.

albumen and casein would be absorbed in far too small a quantity from the intestinal canal to suffice for the nutrition of the organism.

An observation made by Bidder and Schmidt,* although not very accurately carried out in all its details, may serve to give further support to the above view. These experimentalists have repeatedly observed that the contents of the thoracic duct did not coagulate for several hours, and then only imperfectly, in dogs in which the pancreatic duct had been closed for a long time, whereas ordinarily these contents become coagulated in a few seconds. Will not this result, if its connexion with the absence of the pancreatic juice in the intestine be confirmed by further investigations, serve to demonstrate that the pancreatic juice itself exerts an action on the metamorphosis of the peptones even after their resorption into the lacteals, and that it probably contributes in some degree to the regeneration of certain albuminates from the peptones? At all events, this observation is in perfect accordance with the result of our experience, that the albumen-like bodies, as emulsin, diastase, &c., are not capable of resorption, as well as with the view, which we have boldly maintained, that the albuminates in their unchanged condition are only resorbed in an extremely small quantity, the greater part of them being previously converted into peptones.

We are as little able to explain the reason why special vessels exist in the organism for the resorption of the digested protein-bodies and their derivatives (that is to say, their peptones) as to recognise the physical conditions which direct these substances, although not exclusively, yet chiefly, to the lacteals in preference to the blood-vessels. To speak candidly, we must confess that we have no definite idea of the mechanism of resorption through the lacteals. All experiments made with the view of explaining the process of absorption by the lacteals, refer solely to the mechanism of the continuous motion of the fluids in them, but not to the true process of absorption. After having formerly determined all the incidental or indirect means by which the motion of the chyle and of the lymph is effected—the special *Vis a tergo* which does not admit of a physical definition—we at length find Brücke's† discovery of fibre-cells in the intestinal villi (a fact which has been confirmed by Kölliker‡), affording a sufficient indication regarding

* Op. cit. p. 259.

† Berichte d. k. k. Akad. d. Wiss. zu Wien. 1851.

‡ Zeitsch. f. wiss. Zool. Bd. 3, S. 106; and Mikrosk. Anat. Bd. 2, S. 158.

the *Primum movens* of the motions of the lymph. Since, moreover, Lacauchie,* Gruby and Delafond,† and more recently Brücke and Kölliker, have witnessed obvious contractions of the villi, we can hardly doubt that it is these contractions which communicate the first impulse to the motion of the chyle in the minutest ramifications of the lacteals. But although the discovery of fibre-cells in the villi has revealed to us the mode in which the commencing branches of the lymphatics are emptied, we have as yet made no advance towards the explanation of the manner in which these minutest lymphatic branches become filled. We have already mentioned that the capillaries of the villi present a closer resemblance than the lacteals to the root-fibrils of plants, in so far as absorption is concerned. In the lacteals there is neither any fluid which is so concentrated, nor any substance which is so soluble, as to occasion an attraction of the fluids from the intestine; and indeed the apices of the lacteals do not even float in the intestinal fluids, which must pass through several series of cells, and then come in contact with the minute capillaries, before they reach the true lacteals. One might almost wonder that, considering how great the absorbing power of the blood-vessels is, and that all the fluids must pass over them, so much important nutrient matter can find its way into the lacteals. It would appear, therefore, as if only those matters were taken up by the lacteals which the blood-vessels can only absorb with difficulty, or not at all. From these considerations, based on anatomical structure, as well as from certain experiments which showed that many membranes are only permeable for certain substances (as, for instance, caoutchouc for spirit, and not for water, the bladder of the pig for water, and not for spirit, &c.), we have been led to believe, with Lotze,‡ that the coats of the blood-vessels on the one hand, and those of the lacteals on the other, have a specific action, and allow one substance to pass through them, but not another. But even if we assume that there is such a specific difference in the membranes in question, we yet obtain no explanation as to the special agent which forces the matters through the walls of the lymphatics. The walls of the lacteals present opposition to the substances which are heterogeneous to them, but they do not on that account attract those by which they are permeable. The assumption of a

* Compt. rend. T. 16, p. 1125.

† Ibid., p. 1195.

‡ Allg. Physiologie. S. 260.

specific permeability of the membranes does not, therefore, clear up the obscurity regarding the absorption by the lacteals.

We may not, perhaps, have sufficient grounds for the assumption of an altogether special (or specific) permeability of the different membranes; we may well suppose that differences in their thickness, tension, and other purely mechanical relations render the membranes, which in a chemical point of view are analogously constituted, more or less permeable for physically and chemically differing substances, so that no individual membrane could be characterised as absolutely impermeable. Independently of the great similarity in the chemical constitution of these animal membranes, those experiments on the resorbability of certain substances (poisons) through the blood-vessels or lymphatics, which have given rise to so much literary discussion, are opposed to the absolute impermeability of a membrane for the passage of certain matters. Thus, for instance, it appears to us that, contrary to Henle and Dusch's* view, it has been tolerably well proved by the numerous experiments of Bischoff,† Ludwig,‡ and Stannius,§ that the lymphatics can absorb strychnine, and convey it into the blood, although far more slowly, and in smaller quantities, than the capillaries. Hence we also believe that the caution which is so necessary in this part of our inquiries demands that, instead of assuming that a perfectly specific relation is shown by different membranes towards different solutions, we should admit nothing more than gradual differences in this respect. On this account we have not ventured to maintain that albumen and fat, for instance, are solely resorbed through the lymphatics, whilst salts and alkaloids are alone resorbed through the blood-vessels. We must not forget, in endeavouring to form some idea of absorption from these experiments, that, on the one hand, we may probably still be ignorant of the physical laws by which those molecular motions are to be explained, and that, on the other hand, we may not be sufficiently well acquainted with the course of those phenomena which manifest themselves in the villi and in their elements during absorption. The comprehension of these phenomena is so extremely difficult, that even the best observers are not agreed in reference to many of them. It must be further borne in mind that chemical as well as molecular movements are here brought

* Zeitschr. f. rat. Med. Bd. 4, S. 368-374.

† Ibid. Vol. 5, p. 293.

‡ Ibid.

§ Arch. f. physiol. Heilk. Bd. 9, S. 23.

into play; but when we assume the concurrence of mechanical and chemical movements, we do not take into consideration the metamorphoses which the chyle undergoes in the vessels themselves before it reaches the subclavian vein. Still less would we refer to the very hypothetical conversion of sugar into fat within the villi; but we might be led to conclude, from the striking difference in the optical appearance of the cells described by Weber, that, in addition to the mechanical absorption, certain chemical alterations actually occur in the villi; thus, for instance, if we find in a certain portion of the intestine many strongly refracting vesicles, we shall also find, somewhat higher up, where the absorption is half completed, many others which are granular and dark (appearing white in incident light), and some of which are partially filled with a granular, and others with a lighter mass; and still higher up in the intestine we find only cells which are filled with granular matter. No conclusions ought to be drawn from these experiments of Weber, which we have only quoted for the purpose of showing that, even in an anatomical point of view, there is much to be done before we can hope successfully to arrive at any explanation of the process of resorption.

Bidder and Schmidt have at all events the merit of being the first to determine directly the *quantity of fluids* which are poured into the intestinal canal as *digestive agents*. The result of these investigations very considerably exceeds all the assumptions which had hitherto been made in reference to the amount of any of the secretions; who could have conceived, or ventured to assert, that the juices which flow into the intestinal canal in the twenty-four hours amount to almost the sixth part of the whole weight of the body? If we apply to the case of an adult man the quantitative relations of the individual secretions obtained for animals according to the above data, by Bidder and Schmidt, it follows from their calculations, that a man whose weight is about 64 kilogrammes [or about 10 stone] will secrete in the 24 hours,

Saliva	amounting to	1·6	kilogrammes,	containing	15	grammes of solid matter.
Bile	„	1·6	„	„	80	„
Gastric juice		6·4	„	„	192	„
Pancreatic juice		0·2	„	„	20	„
Intestinal juice		0·2	„	„ about	3	„

The quantity of fluid which passes from the blood into the intestine during the 24 hours is therefore far larger than the amount of blood which, according to the most probable recent determina-

tions, is contained in the body of an adult. This mass of fluid, which contains only 310 grammes of solid constituents (and therefore, 3·1%) is especially designed to rinse and purify the absorbed food; and hence we may take the view, long since adopted by Berzelius, that digestion is a true process of rinsing. But however obvious the aim of this abundant secretion of aqueous fluid may be, since it not only favours the solution of the food, but essentially contributes towards its resorption, we ought not to forget that it at the same time imparts an extraordinary motion to the fluid masses within the animal body. The blood within the vessels not only circulates in the course of a few minutes through the whole of the body, but it also carries a considerable mass of fluid into the intestinal canal, from whence, in a longer or shorter time, it is again almost entirely restored to the vessels. This continuous ebb and flow of aqueous solutions can scarcely fail to exert an influence or to react upon the processes of nutrition and metamorphosis generally, which originate in the blood. We might perhaps have formed some idea of these relations from what we learnt of the destiny of the bile in the organism after its secretion, and of the purposes which the formation and secretion of bile were designed to fulfil in the intermediate metamorphosis of matter. We have seen that the bile is poured into the intestine in order to be again almost completely resorbed; and we have found that not only its water repeatedly circulated through the portal vein, liver, and intestine, but also that its solid constituents were for the most part returned into the blood through the lymphatics. A portion of the organic matters must, therefore, first pass through the stage of biliary formation, and then return from the intestine into the blood, in order that it may be applied to further purposes. As the bile shows itself to be not merely a simple secretion, designed for the digestion of definite substances, so also the other secretions, which are poured in such abundance into the intestine without leaving a trace of their solid or fluid constituents in the excrements, may serve to carry away with them from the blood into the intestine different substances which have become temporarily effete, in order that they may be carried back to the blood after having been subjected to metamorphosis, and rendered available for further purposes.

This transfusion of certain substances into the secretions, and their return into the blood, is not limited to the normal organic and inorganic constituents of the secretions; for we find, after the copious transfusion of water into the blood, that not only is the

quantity of water in the secretions increased, but that there is often a simultaneous augmentation of their solid constituents, which are separated with them from the blood. The effete matters undoubtedly often pass through this course more than once; thus we frequently see iodide of potassium pass into the saliva (as witnessed by myself), ferrocyanide of potassium into the gastric juice (Bernard), arsenic, lead, and copper into the bile (Meurer and others), and iron into the intestinal juice (Buchheim), all of which often remain a very long time in the organism before they are returned to the external world through the special organs of excretion. The elucidation of the above relations is perhaps one of the most important among the numerous interesting contributions to science which have resulted from the investigations of Bidder and Schmidt, who have conducted these inquiries with equal intelligence and perseverance. We shall revert to this subject under the head of "Nutrition," when we shall have to consider the intermediate metamorphosis of matter—that process which to a certain degree is effected in the living organism, independently of absorption and excretion.

Important to physiology as is the knowledge of the influence exerted by the *nervous system* on the molecular movements in the animal body, yet an inquiry of this nature, strictly speaking, scarcely belongs to the domain of physiological chemistry, seeing that we are still entirely ignorant of the chemical phenomena which are associated with the function of the nerves. Since, however, in the establishment of theories regarding animal metamorphosis, the existence of the nerves and their influence on the individual factors of this process have been almost entirely ignored from a chemical point of view, it might not be wholly out of place were we here to observe, that the more recent physiological investigations have established beyond all doubt the direct dependence of certain secretions upon definite parts of the nervous system.

We have already frequently had occasion to refer to Ludwig's* important investigations in relation to the secretion of the saliva. It appears from these observations, that there is not the slightest amount of saliva secreted independently of the influence of the nerves, and that the secretion is not effected indirectly by nervous excitation, that is to say, through the agency of contractile parts or by increased pressure of the blood-vessels, but directly through the special influence of the nerves.

* Op. cit. and Zeitschr. f. rat. Med. N. F. Bd. 1, S. 255-277.

The direct influence of the facial nerve upon the secretion of the parotid gland, the indirect action of the third branch of the fifth pair (by inducing the movements of mastication), and the reflex action through the glosso-pharyngeal nerve, have been investigated in rabbits by Rahn,* under the direction of Ludwig, with all the acuteness of experimental criticism.

Ludwig's admirable investigations afford some grounds for the belief, that all those secretions which only appear at certain times or in consequence of definite excitants, as for instance those of the gastric juice and of the pancreatic fluid, are only produced under the action of certain groups of nerves. The correctness of this view, in reference to the two last-named animal juices, seems to be confirmed by the observations recently repeated by Bidder and Schmidt,† that the gastric juice is copiously effused into the stomachs of dogs when flesh or any other attractive food is placed before them while fasting. But although we certainly cannot deny the influence of the nerves upon the secretion of the gastric juice, we are entirely unable to determine upon which nerve this secretion depends. It has generally been referred to the pneumogastrics, and in recent times with more certainty, since Ed. Weber's‡ admirable experiments (of which I was myself a witness) have proved beyond a doubt that these nerves exert a direct influence on the contractions of the muscular coat of the stomach. The direct observations which have been made in reference to the secretion of the gastric juice after the division of both the pneumogastrics have, however, led to entirely opposite results. Whilst Arnold, Reid,§ Leuret and Lassaigne, as well as Longet,|| following the views of Joh. Müller¶ and Dieckhoff,** could not perceive any change in the character of the secreted gastric juice in consequence of the division of the pneumogastric nerve, Bouchardat and Sandras,†† and subsequently to them Bernard‡‡ and Frerichs,§§ believed that they had convinced themselves that no acid gastric

* Zeitschr. f. rat. Med. N. F. Bd. 1, S. 285-292.

† Op. cit., p. 35.

‡ Handwörterbuch der Physiologie. Bd. 3, Abt. 2, S. 41.

§ Edin. Med. and Surg. Journ. Vol. 51, p. 310.

|| Arch. gén. de Méd. T. 15, p. 230, and Compt. red. T. 14, p. 266.

¶ Handb. d. Physiol. Bd. 1, S. 459 [or English Transl. 1839, Vol. 1, p. 597.]

** De actione, quam nervus vagus in digestionem ciborum exerceat, Diss. inaug. Berol. 1835.

†† Revue méd. Fébr. p. 159-180.

‡‡ Compt. rend. T. 18, pp. 783 et 995.

§§ Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 822-825.

juice was any longer secreted after the interruption of continuity of the pneumogastric nerves in the neck, and that there was no longer any true digestion of the albuminates in the stomach (whilst the digestion in the small intestine continued its undisturbed course after such operations). In order more clearly to demonstrate this circumstance, Bidder and Schmidt* instituted very careful experiments on four dogs, in which fistulous openings into the stomach had been made; the result of these experiments was, that the quantity and the composition of the gastric juice, which was secreted after the course of the pneumogastric nerves had been interrupted, was precisely the same as in the normal state. In two cases, however, the quantity and the acidity of the gastric juice were not inconsiderably diminished, but after such an operation as the division of the pneumogastric nerves, so many of the vital functions of the animal become involved, that this diminution can only be regarded as an indirect effect of this action, more especially as in both the other cases a more abundant and more acid gastric juice was secreted than is even commonly observed in the normal state. Independently of the fact that the proportion and character of the constituents, both organic and inorganic, were entirely the same in the gastric juice after division of these nerves as before the operation, the above-named observers convinced themselves that such gastric juice, both within and external to the stomach, possesses precisely the same digestive powers as the ordinary secretion. Are we, then, justified, from these thoroughly exact experiments, in entirely denying to the pneumogastric the function of presiding over the secretion of the gastric juice? We believe not: for even the movements of the stomach, whose dependence on the pneumogastric has been quite decisively established, first by Weber, and subsequently by Reid, Bischoff,† and Volkmann, may often be perceived with scarcely any diminished intensity after division of the pneumogastrics. A nerve whose fibres form so abundant a net-work around the stomach can, however, hardly exert no influence either on its movements or on its secretion, especially when we recollect that Bidder and Schmidt have found that it is in no way connected with the sense of hunger. Volkmann‡ has certainly been led, from anatomical considerations, to the opposite view, in his experiments on the influence of the pneumogastric on the movements of the stomach,

* Op. cit. pp. 90-97.

† Müller's Arch. 1838, S. 496.

‡ Handwörterbuch der Physiologie. Bd. 2, S. 584.

and there is this much in support of his views, that this nerve loses the greater part of its cerebro-spinal fibres within the cranium and in the upper part of the neck, and that its sympathetic fibres increase in proportion to its distance below the diaphragm; hence the pneumogastric in the abdomen is altogether different from the pnuemogastric as it emerges from the cranial cavity; the pneumogastric nerve in the abdomen contains fibres which cannot be irritated from its cervical portion, and whose action on the movements of the stomach cannot therefore be interrupted by dividing the nerve in the neck. In reference to this point, the same remarks are equally applicable to the movements of the stomach and the secretion of the gastric juice. It is, however, clear that further experiments, of an extremely difficult character, are requisite in order to decide the question on what nerve or group of nerves the secretion of the gastric juice directly depends. We must hope that the ingenuity of Ludwig may as brilliantly overcome these difficulties as those which were presented to him in the investigation of the salivary secretion.

Having considered the process of digestion in its most diversified conditions, and noticed the relations between the objects to be digested, the digestive agents, and resorption, it only remains for us to make some observations in reference to the *digestibility* of those objects which, in reference to the nutrition and regeneration of the animal body, have been named "compound," in contrast with the above-mentioned simple nutrient matters. There was a time when, notwithstanding the little that was known of the process of digestion, the digestibility of different more or less compound nutrient matters was a favourite subject for writers to expatiate upon. We shall see, however, that the further we advance in science, the more do we become distrustful of our own experience, and the more modest will be our pretensions. Whilst in former times the most decisive hypotheses or conjectures were unhesitatingly adopted in the absence of all direct observations, and merely on the strength of certain traditions, which, without having been tested, were derived in part from antiquity, the edicts of the schools of the middle ages, or even from the mere biassed notions of the people; we at the present day scarcely venture to give a decisive reply to the simplest and most ordinary questions regarding the digestibility of any nutrient substances, although we may be far removed from that forced scepticism which has in part become the fashion in medicine. Yet what, properly speaking, do we understand by the digestibility of a nutrient substance?

The simplest mode of comprehending this idea will be to understand by the expression the facility with which the nutrient fluids are able to prepare the substance for resorption, or the shortness of the time in which the substance in question undergoes resorption, that is to say, the time at which it disappears from the intestinal tract. Yet how did inquirers formerly endeavour to decide the readiness and rapidity of the metamorphosis of nutrient matters? The determination of this question was mostly limited to this,—that the digestibility of compound nutrient matters was estimated by the subjective feelings which patients or convalescents experienced after having partaken of them. Even if we do not take into account the innumerable deceptions which must necessarily be liable to occur, either on the part of the subject of the experiment or of the person watching the result, an organism which is not in a state of health, and in which all the functions are not performed in a regular manner, cannot assuredly afford a measure of the greater or less digestibility of a substance; for the power of a patient to bear one or other article of food must depend upon the nature of his malady. Thus, for instance, it is *à priori* obvious that one patient will find no difficulty in bearing certain kinds of food, which may induce indisposition in another individual; and every physician who has made it a point at the bedside to attend to the effects of different nutrient substances, as well as to observe the actions of medicines, must be familiar with innumerable instances of this kind. Experiments of this nature are, moreover, not practicable in the case of healthy persons, since they are not conscious from any sensations within themselves whether digestion is proceeding with slowness or rapidity. It is only in recent times, since we have begun to experimentalise scientifically, that attempts have been made to collect any definite positive facts, with the view of establishing the different digestibility of even the most ordinary articles of diet. Of this class of experiments, those of Gosse are the best known; he possessed, as is occasionally the case, the faculty of swallowing air, and of thus distending the stomach to such an extent as to induce vomiting; and he employed this peculiar power in order to bring up food which had remained for different lengths of time in his stomach. Spallanzani* introduced perforated tubes or linen bags filled with different varieties of food, through the œsophagus into the stomachs of cats, and observed in this way the time that elapsed before the various articles of food disappeared from the above-

* Versuche über d. Verdauungsgeschäft Leipz. 1785.

named receptacles. Beaumont* instituted a very extensive series of experiments, regarding the digestibility of different kinds of food, on a man (Alexis St. Martin), in whom there was a very considerable persistent opening from without into the stomach, in consequence of a gun-shot wound. Although Beaumont's investigations have led to many brilliant results in relation to gastric digestion generally, and have much facilitated the path for further inquiries, they do not yield many certain results regarding the question we are now considering. In the first place, all these experiments have reference solely to the time during which the food remains in the *stomach*, although we know that vegetable matters undergo their principal changes in the small intestine, and that a great part even of animal food leaves the stomach in an undigested state, and is only thoroughly digested by the intestinal mucus. These experiments would, however, have been of higher scientific interest, if only the time during which the food remained undigested could have been accurately determined ; Beaumont has, however, generally (and Gosse always) regarded the gastric digestion as ended when the food in the stomach had been converted into an uniform pulp (*chyme*). But even this very uncertain determination would have its own peculiar value, if the experiments both of Gosse and Beaumont were not wanting in two essential points. They used very complicated, variously prepared, and for the most part half vegetable and half animal food, in their experiments (thus, for instance, Beaumont generally gave bread and vegetables with meat) ; and it is at once obvious that such a method is totally unfit for determining the digestibility of individual articles of diet; since Beaumont neither employed chemical means nor the microscope for the minute investigation of the matters that were presumed to be digested, he was naturally unable to decide which constituents of the food were dissolved, which were partially digested, and which were altogether unaffected. Independently of certain other circumstances which should be taken into consideration, it is obvious that only a moderately satisfactory conclusion could have been drawn from Beaumont's experiments if he had employed the simpler articles of food, as albuminates, flesh, meal, bread, &c. His conclusions, even in that case, would less have had reference to the digestibility of individual substances, than to the time in which they are retained in the stomach. The retention of the food in the stomach is, how-

* Experiments and observations on the Gastric Juice and the Physiology of Digestion. Boston, 1834.

ever, extraordinarily different even for one and the same substance, as, for instance, flesh, without our often being able to discover the cause of the difference; this being a point which daily observations on dogs with gastric fistulæ have placed beyond a doubt. It very much seems to depend on the quantity of the food taken at once; if, for instance, we allow a dog to swallow a large quantity of flesh, fragments may be still found in its stomach after six, eight, and even ten hours, while smaller quantities often disappear after less than two hours. And a further reason why the results of Beaumont's observations cannot be specially applied to physiology or even to dietetics, depends upon the circumstance that he has either not at all or very inaccurately described the quantity of the food that was taken; and upon this circumstance may partly depend the great differences which are often observed in his observations, when made under apparently similar conditions.

There are still to be mentioned the experiments instituted by C. G. Schultz,* who at a certain time after feeding dogs and cats with different kinds of food, killed them and examined the contents of their stomachs. These attempts, from the method by which they were carried out, would deserve great confidence if their results did not differ in so remarkable a manner from those obtained by Beaumont and others, that we are almost compelled to presume that there must have been some essential errors in them. The same is the case with the observations which Lallemand instituted on men with gastric fistulæ. Blondlot who first introduced into physiology the operation of artificial gastric fistula was so far from being able to attain to definite results, notwithstanding that his observations were made under far more favourable conditions, that he was led to express the view that the digestibility of different articles of diet depended solely on the state of the stomach at the time of the experiment, and that it is pure waste of time to labour at the determination of the digestibility of individual articles of food.

These few instances are sufficient to indicate that moderately accurate determinations of the digestibility of varieties of animal food are involved in extraordinary difficulties even in relation to gastric digestion alone. At the present time we possess few experiments which can afford a fixed point of departure for the determination of the digestibility of different kinds of food.

My personal experiments, which have reference partly to dogs,

* De alimentorum concoctione experimenta nova. Berol. 1834.

† Traité de la digestion, p. 383-409.

in which gastric fistulæ had been formed, and partly to animals that were killed (generally with a view to other investigations) at definite times after taking food, are limited to the following facts, which increase rather than diminish the uncertainty of our knowledge.

As in the first place we shall only consider the retention of food in the stomach, we shall commence with the digestibility of the albuminous substances.

With regard to *soluble* coagulable *albumen*, it has been already mentioned (see vol. ii, p. 54) that, according to my experience, this substance undergoes a change in the stomach, and is not resorbed unchanged, as Frerichs maintains. Blondlot saw the white of 4 eggs entirely disappear from the stomach in the course of 2½ hours. We can here very distinctly observe the influence which the quantity exerts on the relative digestibility of the food; if we introduce the white of one egg into the stomach of a dog with a gastric fistula, but otherwise healthy, after it has fasted for about 12 hours, we often find in the course of an hour no remaining trace of coagulable matter; but we are more certain to find such traces when the white of two eggs has been taken. If the white of eight or more eggs was given to the same dog, which was one of average size, weighing about 5 kilogrammes [or 11 lbs.], coagulable matters could always be recognised in the stomach after 3 or even after 4 hours, except in cases in which the dog had vomited a portion of the substance.

Densely coagulated *blood-fibrin* requires a longer period for gastric solution than the same substance in a finely comminuted state; a fasting dog swallowed 9·5 grammes of the moist fibrinous crust (buffy-coat) obtained from coagulated horses' blood, and after 2½ hours fragments of it were still contained in the stomach; the same quantity of blood-fibrin obtained from the red coagulum of horses' blood disappeared, with the exception of a few flakes, from the stomach of the dog in the course of 1½ hours. It might have been expected from the simplest chemical experiments, that the degree of cohesion would essentially influence the more or less easy digestion of a substance, and this view is thoroughly bore out by further direct investigations. Fluid, finely divided, porous foods are much more open to the action of the digestive juices, and must necessarily be more readily digestible than others which do not possess these properties in an equal degree.

In order to determine the digestibility of *coagulated albumen*, we

have recently so far modified the experiments of Spallanzani, who introduced the food enclosed in muslin bags through the gullet into the stomach, as to introduce into the stomachs of dogs, through fistulous openings portions of coagulated white of egg of definite form and definite weight, inclosed in similar muslin bags. This method of procedure, which has been adopted by Bidder and Schmidt, as well as by Buchheïm,* may be very advantageously employed in various investigations; the sole objection to it is that we can only employ extremely small quantities of the substance in question, and that even portions of the same albumen often require very different times for their solution; this difference appears to depend as much on the varying density of the albumen (which may certainly differ even in one and the same egg), as on the different positions which the bag containing the albumen may happen to assume in the stomach. In Buchheïm's experiments, which were made with cylindrical pieces of albumen weighing 1 gramme (the stomach having been filled three or four hours previously with bread and curdled milk), it was found that in 1 hour sometimes more than 59%, and in 2 hours even 93% of the originally introduced moist coagulum of albumen were dissolved, although the amount was frequently far smaller. Here again we must give the widest scope to the idea of digestibility; in 1 hour half of the compact mass of coagulated albumen, which presented comparatively little surface, was dissolved, while the gastric digestion previously took from 3 to 4 hours. Further experiments show us, that far more coagulated albumen is digested in 1 hour in the stomach of a dog, when that organ is empty, or when a long time has elapsed since the last meal was taken, than under opposite conditions,—when albumen in small portions, or finely comminuted, is introduced into the stomach than when a cylinder of albumen, of a gramme weight, is introduced,—when a freer motion is permitted to the pieces of albumen than was possible when they were inclosed in bags,—and lastly, when the experiment is instituted on a perfectly healthy dog than when made on dogs with fistulous openings. Hence we may foresee that large pieces of coagulated albumen and long boiled or more or less dried albumen, must require a comparatively long time for their solution, especially when the stomach has been very much filled with food, and digestion has been going on for some time. Hence, independently of many other relations connected with special idiosyncrasies, it is extremely difficult, if not impossible, to find any definite unit of conditions, according to

* Beiträge zur Arzneimittellehre. Leipzig, 1849, S. 15-112.

which a scale of the relative digestibility of different articles of food might be made out. And even if all the conditions were similar, a doubt would always remain as to the precise moment at which gastric digestion might be said to terminate. There can be no definite rule regarding the beginning of digestion, for the solvent process commences as soon as the gastric juice comes in contact with the object to be digested: if, for instance, we allow albumen which has been previously carefully rinsed with acetic acid to remain only five minutes in the stomach, a careful weighing will generally (although not always) indicate a loss, which in this case can only depend on actually digested albumen; a portion is, therefore digested in the course of five minutes, or, at all events, a quarter of an hour, which shows that albumen obviously may be digested in so short a time. We find, however, that when coagulated albumen is introduced in considerable quantity into the stomach, remains of it may sometimes be detected in that organ, even after five hours; as we cannot regard the commencement of the process as affording a measure of the digestibility, the terminations may probably serve this purpose. But even the end cannot be always accurately determined; for while one part of the albuminous body commonly leaves the stomach in an undigested state, another often remains for a long time in the stomach, in consequence of the digesting force of that organ becoming gradually weakened, and its glands secreting less juice after it has been for some time in a state of functional activity—a circumstance which more than any other, is dependent on the individual constitution. In many animals, however, the stomach is never altogether empty, as for instance, in the rabbit. Even when these animals perish from hunger, the remains of their last meal may still be found in the stomach. Although this is not the case with the carnivora and omnivora, it shows that the termination of gastric digestion and the emptying of the stomach cannot furnish any appropriate standard for the determination of the digestibility of a substance. It might perhaps appear superfluous to devote so much space to the consideration of a subject which is so simple of comprehension, but we must bear in mind these relations and the general vagueness of the idea in question, before we can even attempt to construct any scale of the digestibility of the simple and compound articles of food, which could be of use for purely practical purposes. C. Schmidt has never found all the albumen dissolved in the stomach, and after it had remained for six hours inclosed in muslin bags, he constantly found that half of it was still

undissolved; similarly small quantities of albumen, when introduced into an empty stomach without being enclosed, never remained as long as six hours in that organ, but passed for the most part in an unchanged state into the intestine. Beaumont assumes from his observations, that the average period of digestion for hard-boiled eggs is about $1\frac{1}{2}$ hours.

Frerichs has already shown by experiments on living animals, that *boiled fibrin* is dissolved in the stomach far more slowly than the *unboiled* material; we arrive at the same result when both kinds of fibrin are treated externally to the organism with natural or artificial gastric juice.

It is a well-known fact, to which we have already frequently referred, that soluble *casein*, as it exists in milk, is very rapidly coagulated by the gastric juice, and then only very gradually redissolved or digested; casein must, therefore, be the most indigestible of the unboiled protein-substances; a difference is, however, even here observable, according to the more porous or dense condition of the coagulum, for, as we have already remarked at vol. ii, p. 55, the more gelatinously coagulating casein of women's milk is, according to Elsässer, much more rapidly digested than that of cows' milk, which forms in the stomach a compact lump, generally coagulated into a single ball. Frerichs found that clots of casein disappeared from the stomachs of cats and dogs in about $2\frac{1}{2}$ hours. Beaumont, according to his observations, fixes a period of 2 hours for the digestion of milk. Gosse classes milk amongst the most easily digested articles of food, which include, according to him, substances which are converted into chyme within 1 hour or $1\frac{1}{2}$ hour.

Gelatin belongs to those substances which are most readily liquefied in the stomach; in Beaumont's experiments all the gelatinous character of this substance disappeared after it had remained for 20 minutes in the stomach; at the close of an hour no trace could be found in the stomach of 150 grammes of jelly which had been taken. The digestibility of *the gelatigenous tissues* depends, however, entirely upon their aggregate condition, and is very considerably facilitated by their being previously boiled. Frerichs saw the connective and fatty tissues (when inclosed in a thin muslin bag) perfectly dissolved in the stomach of a dog in 60 or 90 minutes after its introduction. It is obvious that tendons and cartilage, and those tissues generally which are abundantly intersected with elastic fibres, belong to the least easily digested class of substances, for we often find these parts only slightly altered, even in

the excrements of the carnivora. True elastic tissue and elastic fibres completely resist the action of the digestive fluids.

Chemically pure *syntonin* appears, from several experiments which I have made, to be very readily digested, its digestibility being in fact greater than that of the blood-fibrin of the ox; when in a state of coagulation, it is tolerably similar in this respect to coagulated albumen and casein. Although this substance is perfectly identical in every kind of flesh, and also in the smooth muscles (see page 68), experience teaches us that the digestibility of the smooth and of the transversely striated muscles, and even of the latter in different animals, is extremely different. When we consider the histological conformation of these two kinds of muscle, we can readily comprehend why the flesh of organs which consist of smooth muscles is far more easily digested than the transversely striated muscles; we know that the smooth muscles are not provided with the same dense and insoluble, although thin investment (see p. 85) which encloses the primitive bundles (and consequently the syntonin) of the transversely striated muscle, but are for the most part surrounded only with loose connective tissue, which is easily permeated and dissolved by the digestive juices. Hence it was that Beaumont found that tripe disappears with such rapidity (in an hour) from the stomach, and that oysters disappear at all events more quickly than beef and other kinds of meat. The difference in the digestibility of the flesh of different animals is probably for the most part dependent upon mechanical conditions, which are modified by the histological arrangement of the different elementary tissues. Thus the flesh of young animals is more easily digested than that of older animals, for (as we have seen at p. 89) the primitive bundles of the former are far thinner than those of the latter, and on this account they present, in relation to their mass, a larger surface to the gastric juice than a similar piece of meat of equal size, taken from an older animal. Frerichs found that the flesh of old animals required (for its digestion) an hour or an hour and a half longer than that of younger animals. Fish is probably not easily digested (by persons whose digestive powers are not strong) since when introduced into the stomach in a state of fine comminution, and in contact with fluids, it forms an almost homogeneous mass, which can only be slowly acted upon by the digestive fluids from the surface inwards. This is indeed, as Frerichs has shown, more or less the case with every kind of flesh which is gradually acted upon from the surface,

for it is not till the connective tissue has been dissolved that the gastric juice is able to act, through the openings made in it, upon the sarcolemma and primitive bundles (see vol. ii, p. 127). On this account, true muscle does not actually belong to the class of easily digested substances. Frerichs found in the stomach of a cat, four hours after feeding, pieces of raw beef which were only softened on the surfaces. When portions of flesh, inclosed in a fine muslin bag, were introduced through a fistulous opening into the stomach of a dog, they did not thoroughly disappear until after an interval of from five to eight hours.

It has generally been regarded as an established fact that raw flesh is much more difficult of digestion than boiled or roast meat; the difference is not, however, very considerable, and it has been estimated by Frerichs at only half an hour. Nor need we wonder at this, for the advantage derived from the boiling or roasting, by which the connective tissue is loosened and the organic structure is partly destroyed, is in part counteracted by the albumen of the muscular juice as well as the syntonin being reduced to a state of coagulation. The above-mentioned jelly-like swelling-up of the syntonin in acid fluids may, perhaps, in a great measure contribute towards the difficult digestibility of raw meat.

We have formerly had occasion to observe, that after an animal diet, muscular fibres, although in various phases of metamorphosis, may be distinctly recognised along the whole course of the intestinal canal; hence we see that the digestion of flesh is by no means completely effected in the stomach, and that its most important histological element, the true muscular fibre, in association with the sarcolemma, resists for the longest period the action of the digestive fluids; indeed, during an abundant flesh diet, we find a large number of muscular fibres, morphologically unchanged, in the excrements. Hence in the case of flesh we can form no conclusion regarding its digestibility from the duration of its retention in the digestive organs. When dogs are fed solely with flesh, we find that after 6 or 8 hours the greatest part has usually disappeared, although small portions often remain in the stomach for 10 or 12, or even 16 or 20 hours. In their observations on a dog with a fistulous opening at about the middle of the small intestine, Bidder and Schmidt found that most substances escaped in 5 or 6 hours after a meal; and very similar results were observed in a man who was a patient in our hospital, and in whom there was an intestinal fistula at the end of the ileum. We may therefore assume that in the normal state the stomach is not engaged in the

digestion of flesh for a much longer period than four or five hours; and this view coincides tolerably closely with the experiments made by Beaumont. Thus, for instance, he found that boiled lamb disappeared from the stomach after $2\frac{1}{2}$ hours, boiled beef after $2\frac{3}{4}$ hours, roast beef after 3 hours, and broiled beef after 4 hours; on the other hand, roast pork did not disappear from the stomach for $6\frac{1}{2}$ hours, while broiled pork disappeared after $3\frac{1}{4}$ hours. If we are able, in some cases, to adduce scientific explanations for certain practical dietetic rules which accord tolerably well with Beaumont's observations, the far more considerable differences which present themselves in all results of this kind seem to invalidate such conclusions; hence we do not venture to enter minutely into the influence which the different modes of preparing the food, and the different species of animals, exert on the digestibility of the flesh. We must, however, not altogether omit to mention (what has so often been prominently brought forward) that flesh which has been kept lying in vinegar is rendered more digestible, since, as every microscopist knows, the connective tissue and muscular fibre are thus rendered of looser texture; and that smoked meat is generally far more difficult of digestion than unsmoked, since the pickle in which the meat was placed preparatory to the smoking not only extracts from the flesh a fluid containing certain easily digestible substances, but also renders the fibres themselves harder and more insoluble.

With regard to the *fats*, it is tolerably well agreed that they rank amongst the most indigestible matters; physicians have, indeed, always exhibited an extraordinary aversion to permit the use of fatty food to any of their patients, although they see that many fats, as, for instance, the fashionable, but generally rancid, cod-liver oil, is very easily digested. It may readily be conceived from its physical characters, as, for instance, its insolubility in water, and the resistance which it offers to the most powerful reagents, that fat, as compared with the other simple nutrient substances, is only slowly absorbed; indeed, even to the most recent times, it has been difficult to form an idea of the mode in which fat undergoes resorption. It is sufficiently clear, from what has been previously stated, that the stomach is not the place where the fat is resorbed, or even where it undergoes any essential changes; but when it is taken in large quantity, either alone or with other food, it usually remains for a long time in the stomach; thus Beaumont found beef-suet in St. Martin's stomach after $5\frac{1}{2}$ hours. It is not only not digested in the stomach, but often exerts

an impeding action on the digestion of other substances in that organ, since, on the one hand, it liquefies in consequence of the high temperature, and, encasing as it were the individual particles of food, renders them proof against the digestive juices ; and since, on the other, it becomes rancid during its long retention at that temperature, and forms volatile acids, which exert a very deleterious, although not duly investigated, action on digestion. It must, therefore, be admitted that large quantities of fat are prejudicial to gastric digestion, although, strictly speaking, there is no digestion of fat in the stomach. The digestion of fat does not commence, as we have already seen, until it reaches the small intestine, and even there it only takes place under certain limitations. We have seen from the accordant experiments of Boussingault on the one hand, and Bidder and Schmidt on the other, that the animal organism can only take up a limited quantity of fat in a given time; after animals were fed upon very fat flesh, we find that there were ejected from the fistulous opening in the intestine (in Bidder and Schmidt's experiments) grey masses which contained an abundance of fat, while only very slight remains of muscular fibres could be detected in them. Hence we can no more draw any inference from the retention of the fat in the stomach regarding the degree of its digestibility than from its passage into the small intestine and the solid excrements. Small quantities of fat meet with the means requisite for their digestion in the small intestine, and are there very rapidly resorbed. If we can draw any conclusion from the distension of the intestinal villi with fat, and the appearance of white chyle in their lacteals, we must regard the fat as very easy of digestion ; for in the course of from half an hour to an hour after fatty food or oil has been taken, we find in the upper part of the jejunum in dogs, cats, and rabbits (as I have very often convinced myself), not merely the epithelium filled with fat-globules, but also the lacteals with glistening white chyle. We have, however, formerly shewn (see vol. i, p. 265) that fat, when not mixed in too large quantity with the food, essentially promotes the digestion both of the albuminous and the amylaceous substances.

It has been already fully shown that most vegetable substances, like the fats, do not undergo gastric digestion ; we cannot, therefore, judge regarding their digestibility from their longer or shorter retention in the stomach, in the same manner as in the case of the albuminous matters. We have already expressed an opinion, founded on our own experiments, and differing from that of

Bidder and Schmidt, that *starch*, the principal nutrient matter contained in vegetables, is in part converted in the stomach into sugar, and even into lactic acid; this metamorphosis of starch within the stomach is, however, so far as we can conclude from our former experiments, solely dependent upon the quantity of the saliva that is excreted; the greatest part of the starch is first metamorphosed in the intestine. We have already sufficiently alluded to the fact that the conversion of this substance in the intestine takes place most rapidly when it is finely comminuted and thoroughly saturated with water (in short, when it is boiled). If we confine ourselves solely to the question of the digestibility of starch, we should regard it as in general easy of digestion, although we very frequently meet with considerable quantities of it passing through the rectum of man and animals. This last-named fact is dependent partly on the circumstance of an excessive quantity of raw (unboiled) starch having been taken (for the saliva, pancreatic fluid, and intestinal juice are not secreted in such quantities, and with such powers, as to metamorphose any amount of starch), and partly upon the fact that the starch is enclosed in vegetable cells, through which the digestive fluid can only enter by endosmosis. Hence the digestibility of *vegetables* depends chiefly on the nature of the cells in which the starch and the vegetable protein-bodies are inclosed; if the cells are still invested with epidermis, no portion of them is dissolved, since the epidermis of plants is completely proof against the digestive fluids. Boiling is so far useful in regard to vegetable food, that it thoroughly loosens the intercellular substance of the parenchymatous cells, and hence allows the digestive juices to make their way more readily between the cells; moreover, the process of boiling causes the outermost layer surrounding the starch-granules to burst, and it is this layer which is the main impediment, in the case of raw starch, to the action of the digestive fluids. Since the protein-bodies occurring in plants exist in a state of the finest comminution, they offer far less opposition to the action of the digestive juices (when the latter once come in contact with them) than the corresponding animal protein-bodies. Hence, moreover, it is easy to see why bread is comparatively so easy of digestion. We must, however, again recur to the fact that in the case of vegetables we are even far less able to draw any conclusion regarding their digestibility, from their longer or shorter retention in the stomach, than in the case of animal food. The most important part of the digestion of vegetables assuredly takes place

in the small intestine, and, to a certain degree, also in the large intestine; for even if, in accordance with the observations of Bidder and Schmidt, we regard the secretion of the intestinal juice in the latter as inconsiderable, the enormous size of the cæcum in most of the herbivorous animals indicates that a very essential act in the process of digestion must take place in this region. The chief difficulty in connexion with the digestion of vegetables, therefore, does not lie in the stomach, and hence their retention in that organ cannot be strictly considered as a measure of their digestibility; and yet vegetables remain on an average longer in the stomach than animal food. Even after feeding an animal with bread, we may find the greater part of it in the stomach after a lapse of 3 hours, and the quantity hardly perceptibly diminishes till after 4 hours (Frerichs), and remains of bread are commonly found in the stomachs of dogs after 5 or 6 hours, and often even after 8 or 10 hours: potatoes and other vegetables remain in this organ for a far longer time; Frerichs, as well as Bidder and Schmidt, have frequently found the remains of vegetable substances in the stomachs of dogs after the lapse of 22 hours; and we have already mentioned that the stomach in many herbivorous animals is never completely empty. If we have thus established the point that the disappearance of an article of food from the stomach affords no proof of its digestibility, the next question that suggests itself is in relation to the conditions under which the stomach either retains or impels into the small intestine the more or less digested matters—a question to which, in the present state of our knowledge, we can give no satisfactory answer. This is one of the least important of the many problems whose solution must be left to future investigators, notwithstanding the admirable and comprehensive labours of Frerichs and of Bidder and Schmidt. We are, however, here forcibly reminded of the fact, that notwithstanding the brilliant triumphs of science in this direction, we have as yet only gained the outworks from which further advances must be made.

As we have limited ourselves in the former pages almost exclusively to the consideration of the principles which, in accordance with the present condition of science, ought to guide us in our judgment of the digestibility of the different articles of food, some of our readers may miss the important aids and special indications they may here have hoped to discover in relation to medical practice; for many physicians seem to entertain the idea that physiological chemistry must be able to decide all questions

of a practical character, and accurately to determine the digestibility of every article of food, or at all events to furnish sharply-defined rules for its estimation; and some have even gone so far as to expect that this branch of our science should serve in every respect as a guide for a system of dietetics. But even if our physiological premises were sufficient for this purpose, and if our positive facts were less deficient than they are, we should consider a text-book of physiological chemistry as an inappropriate place for a comprehensive exposition of the relations involved in this department of science: purely scientific inquiry is bounded by definite limits; the application to practical life of the facts discovered by science must be left to the kindred but less strictly scientific branches of knowledge; all that is required for practical application must be supplied by the methods peculiar to the so-called practical sciences. Thus, for instance, there exists a large amount of material in reference to the digestibility of the different nutrient matters, which appertains exclusively to a medical inquiry. For we do not concur with those who denounce as unfounded every fact which has not been obtained by the exact methods of physical science, and who consequently often arbitrarily cast aside many striking hypotheses which may be advanced by physicians in reference to dietetic conditions; far from participating in such views, we do justice to the fruits which practical experience is able to furnish, and we are fully aware that a physician may do a great deal by the bedside towards the introduction of correct dietetics, without our being able to refer his mode of practice to scientific grounds. Thus, for instance, we know that a number of substances, which present considerable analogy to one another in a physical and chemical point of view, exhibit great differences in reference to their digestibility under certain morbid conditions; there are a number of still more mysterious phenomena known to every attentive physician, which, although they owe their recognition to no exact scientific method, are yet as firmly established as if they were mathematical propositions. Yet the solution of these mysteries—the formation of comprehensive scales for the calculation of the digestibility of different articles of food in accordance with their chemical nature or preparation—and the determination of the causes by which a substance which is in itself easy of digestion may become less digestible under different external or internal relations (for the simple digestibility of a substance must be distinguished from the facility with which a patient is able to digest it)—these are all

questions which it behoves the physician to determine, and which do not fall within the province of physiological chemistry. The latter science merely furnishes the physician with the fixed principles or scientific means necessary for enabling him to arrive at a more exact knowledge of carefully observed practical facts on which to base a system of dietetics. Until the appearance of Moleschott's admirable work,* most of the treatises on dietetics consisted merely of individual physiological facts carelessly connected with more or less well-grounded propositions; and while they were deficient in a logically strict treatment of these different propositions, they did not even give those minute observations with which many of the older practitioners had enriched the theory of dietetics; not unfrequently, indeed, we meet with an entire confounding of the ideas of digestibility, nutritive power, and the facility with which different articles of food can be borne. Such a proper elaboration of dietetics does not, however, fall within the province of physiology, but belongs exclusively to the practical physician.

We cannot avoid offering a few remarks on certain misconceptions which we occasionally meet with in reference to the value of physiological chemistry, in relation to Pathology and Therapeutics. Although we have endeavoured throughout the present work to draw attention to the deficiency of our knowledge, to refer all views and assertions to their true foundation, and to check as far as possible the haste with which individual observations or discoveries have been applied to practice, we have been anxious to avoid those hasty and uncharitable judgments which we meet with from time to time both in literature and in medical practice. Physiological Chemistry has recently done more in destroying former illusions, than in furnishing physicians with new materials for further hypotheses. We may, indeed, instance many discoveries in Physiological Chemistry which have exerted a direct influence on medical practice, but the great number of deficiencies which still exist in this respect, hold out a prospect of ample return to future labourers. It is not the province of Physiological Chemistry, as a special department of science and a branch of physiology, to guide the physician within narrow limits by which he must bound his own reflections and investigations, and regulate his practice; for our science presents too many deficiencies within its own domain to enter upon a foreign province, whose possession has already caused strife and jealousy.

* Physiologie d. Nahrungsmittel. Darmstadt, 1850.

Physiological Chemistry no more constitutes a science of therapeutics and diagnostics, than pure physiology can be said to constitute the science of pathology. Technical Chemistry does not undertake to show what mordant will affect a certain organic tissue, or how the fire of a furnace can be kindled; the noblest discoveries in this department have been made, not by chemists, but by practical men with the aid of chemistry. A similar relation exists between physiological chemistry and the physician; the latter must not remain inactively waiting until physiological chemistry is ready to supply him with a diagnostic agent for every disease which is accessible to its investigation. It is the duty of the practitioner to apply every fresh conquest in the field of science to the benefit of medical practice, and to endeavour to extract by his own researches and labours all the practical results to be obtained from the treasures of science, instead of requiring that, under the pressure of his other avocations, all difficulties should be smoothed from his path, and the results of laborious research presented for his acceptance, cleared from their obscurity and divested of their difficulties.

Respiration.

Although (in the second volume) we have considered the excretions of the animal organism, there is one of the most important of them which has not yet been noticed, namely, that from the lungs. The reason of this omission is obvious, for whilst pulmonary excretion challenges our attention as a process, the quality of the products of excretion does not demand any special notice, as they consist mainly of carbonic acid and water. The full exposition of this subject has been deferred to the present place, since it leads most securely to the development of that which we have already designated as the crowning point of physiological chemistry, to the attainment of which an accurate acquaintance with the process of respiration is indispensable. For since this process reflects almost all conditions of animal life, including even those which are not directly connected with the vegetative process, it not only throws considerable light on individual subjects connected with the nutrition and maintenance of the animal body, but it also furnishes us with the most stable supports for

forming a scientific estimate of the quantitative metamorphosis of matter, and of the entire animal economy. On this account we consider it as the last link in the series in which we have treated of the solid and fluid parts of the animal body and its various functions.

We should greatly err, were we to regard the lungs simply as organs of excretion, for they differ from other excreting organs, inasmuch as they not only excrete gaseous bodies, but also absorb certain elastic fluid substances. An interchange of gases is therefore effected within the lungs. Although our notice of the respiratory process must necessarily be especially directed to the higher pulmoniferous animals, we must bear in mind that that interchange of gases which we term respiration is by no means solely limited to the organs known as lungs. As is well known, there are many aquatic animals besides fishes which breathe through gills, while insects are provided with a system of tubes (tracheæ) which take the place of lungs, and which, like blood-vessels, are distributed through all the tissues on which vital activity depends in these non-vascular animals—a circumstance of great importance in connection with the theory of the respiratory process.

If the respiratory process depends essentially upon an interchange of certain substances within the lungs, an accurate acquaintance with the substances whose constituent parts are thus interchanged is indispensably necessary for the scientific comprehension of this subject. Thus, in considering pulmonary respiration, we must be accurately acquainted, on the one hand, with the constitution of the blood, and, on the other, with the character of the atmosphere, before we can venture to form a judgment regarding the interchange which takes place. We do not, however, purpose entering more fully into the close consideration of these two fundamental bases of the respiratory process, as we have already, in the second volume, considered the constitution of the blood and the amount of gases which it contains; and as we must presume that our readers are equally well acquainted with the chemical constitution of the atmospheric air and with the physical laws of the motion of elastic fluids.

The causes which present themselves to our notice as essential agents in effecting that interchange of gases which takes place in the lungs of air-breathing animals may be of three different kinds, anatomico-mechanical, physico-chemical, and purely physiological, without, however, being fundamentally and completely distinct; for each cause must, from the nature of the case, merge into the

others. We need scarcely observe that the *mechanical momenta* depend upon the manner and the degree in which the bodies acted upon, namely, the blood and the atmospheric air, are brought into contact with one another, and by which this interchange is rendered possible and promoted. We abstain from giving a systematic exposition of the anatomical relations and the entire mechanism of the respiration, since, in the first place, we must presume that our readers have some knowledge of anatomy as well as of pure chemistry, and, in the second, that the following remarks will suffice to afford some idea of these modifications in the quantitative results of the respiratory process, which depend upon differences in the mechanical relations.

In the first place, we ought to observe that no direct communication exists between the fluids which undergo this mutual interchange, for the elastic and fluid atmosphere and the liquid blood, are separated by an extremely delicate moistened membrane. Although the interchange of the gases may be somewhat retarded by these membranes, nature has compensated for these impediments by giving an extraordinary degree of expansion to the surfaces of contact. The extremely delicate distribution of the blood- and air-vessels affords an immense extent of superficies in a small space, and enables the processes to be widely diffused. The fluids, however, do not stagnate at those surfaces (the membranes) which establish communication between them, but both are maintained by very different physical means in continuous motion and in constant interchange; and hence we have an additional condition which essentially facilitates this process. The heart, which, as is well known, sends forth the vessels of the lesser circulation into the lungs, constantly propels new blood through them, and is undoubtedly the most essential agent in circulatingthe blood through these organs; for even though the mechanism of respiration may exert some action on the movement of the blood in the lungs, pathologists have gone too far in maintaining, as some have done, that respiration is the sole cause of the motion of the blood. With regard to the motion of the air, on the other hand, it must be observed that the great increase of surface obtained in a circumscribed space (by the minute division of the air-vessels) renders its interchange with the gases of the blood less easy; we may compare the space filled with air within the thoracic cavity to a cone whose base is extremely large in proportion to its height; the base being constituted by the sum of the surfaces of the pulmonary vesicles, whilst we place the apex in the glottis;

the interchange of air is therefore considerably impeded from the narrow calibre of the glottis being the only means by which air can enter into and be expelled from this wide, conically-shaped cavity. The high diffusibility of the gases certainly contributes in some degree to counterbalance the effect of this narrow opening, and induces no inconsiderable interchange of air, both within and externally to this space; but this motion would be quite insufficient for the purposes of life (excepting in the case of the hybernating animals), and hence special provisions exist for the expulsion of the contained air by a partial diminution of this cavity and for the re-admission of new air by its re-expansion. The mechanism by which this object is effected depends partly upon the peculiar structure of the thorax and the position of the muscles which move it, and partly on the peculiar elasticity of the pulmonary tissue. We should, however, form a very erroneous idea of the motion induced by this mechanism, were we to conceive that it was able to agitate the whole of the air contained within the cavity of the chest. For even when the contraction is relatively considerable, only a small fraction of the air is expelled, and an equally small proportion admitted by its expansion; hence it is only in the wider air-canals that the air can be absolutely changed, whilst in the narrower vessels there is only an undulating current of the stagnant air-column, induced by the contractility of the walls. The change therefore depends solely upon the different degrees of diffusibility of the gases. However simple this latter circumstance may appear, Vierordt has the merit of being the first who experimentally illustrated these physical relations.

A careful consideration of the above-mentioned mechanical relations shows how extensively this interchange of gases must be modified by slight alterations of the external conditions. We must not, therefore, believe that the difference in the characters of the blood and of the inspired air merely influences the final results of this interchange of gases, for it might rather be predicated as a physical necessity, that if the blood were propelled more copiously through the lungs, and the air was more frequently changed in this conical space (the latter being more considerably dilated and contracted), the results of the interchange would be different from what they would be in the opposite case. A more careful study of the mechanism of the respiration will not, however, always enable us to refer the modifications which it presents to proximate causes, based upon chemical and mechanical conditions; for these conditions are themselves often dependent upon so-called physio-

logical relations, whose influence upon the character and motion of the blood, the frequency of the respiration, &c., have not yet been sufficiently investigated. We are, therefore, compelled, in endeavouring to deduce the laws of this interchange of gases, to trace the modifications to which they are liable, to the remote as well as the proximate causes from which they emanate. It is clear from the above remarks, that the proximate causes of those alterations which we meet with in the quantitative relations of the products of respiration are solely based upon the prevailing physical and chemical conditions; the more remote causes, those, namely, of a physiological character, can only influence this interchange of gases inasmuch as they modify those essentially physical and chemical relations. We cannot, therefore, hope to explain the influence exerted by any definite physiological relation on the products of respiration, until we have more clearly established its connection with the physical and chemical fundamental conditions of respiration. For this reason we shall in our further considerations of the process of respiration, at once enter upon the influences which purely chemical and physical relations exert on the interchange of gases, in order thus to elucidate the influence of the physiological conditions. Many difficulties here present themselves, one of the chief of which is the imperfect knowledge we possess of the constitution of the blood in ordinary cases, and the mere conjectural nature of our knowlege of the amount of gases which it contains, although as we have already observed, this constitutes one of the two main factors of this process, and hence we are compelled to enter more fully into these physiological conditions than we should otherwise have done.

We must, however, devote a few brief remarks to the general results of the chemical investigation of the substances which meet together in the act of respiration, before we enter more fully into the causal connection of the modifications of the interchange of gases.

There is scarcely any portion of physiological chemistry which, notwithstanding the great difficulties that oppose its investigation, has been so circumstantially and exactly elucidated as the respiration. It would appear from the works of the older chemists, as Lavoisier and Seguin,* Humphrey Davy,† Allen and Pepys,‡

* Mémoires de l'Acad. de Paris.

† Researches, chemical and philosophical, chiefly concerning nitrous oxide, or dephlogisticated air and its respiration. London, 1800.

‡ Philosophical Transactions for 1808.

Humboldt and Provençal,* Prout,† and others, that attention had not hitherto been directed to this subject, but when physiologists endeavoured to elucidate the mechanism of respiration from all points of view, the chemistry of the process obtained some of the attention which it merited, and the most exact and admirable investigations were at once prosecuted by the aid of the most recent appliances of science. The beautiful experiments of Magnus (see vol. ii, p. 190-192) on the amount of gases in the blood, may be said in some degree to have constituted the turning point in these inquiries, since it is only by the establishment of this factor that we can enter upon a satisfactory investigation of the interchange of gases in the lungs. Numerous investigations, of which the greater number are very admirable, have been instituted both on man and animals with a view of determining the relation between the inspired and expired air. Scharling,‡ Dumas,§ Andral and Gavarret,|| Valentin and Brunner,¶ Vierordt,** Malcolm,†† and Hannover‡‡ directed their investigations for the most part to the excretion of carbonic acid in man under different physical, physiological, and pathological relations. Many of the difficulties which are inseparable from investigations on man, or which influence the accuracy of the method of investigation were happily obviated in the series of exact and highly successful investigations of Valentin, Marchand,§§ Boussingault,|||| Letellier,¶¶ Ph. Zimmermann,*** von Erlach,††† Lassaigne,‡‡‡ myself, and especially Regnault and Reiset.§§§ We are principally indebted to the labours of these chemists for

* Mém. de la Soc. d'Arcueil. T. 2.

† Thomson's Annals of Philosophy. Vol. 2, p. 328.

‡ Ann. d. Ch. u. Pharm. Bd. 45, S. 214.

§ Essai de Physiologie chim., p. 160.

|| Ann. de Chim. et de Phys. 3 Sér. T. 8, pp. 129-150.

¶ Arch. f. physiol. Heilk. Bd. 2, S. 372-417.

** Ibid., Vol. 3, pp. 536-588, and Physiologie des Athmens. Karlsruhe, 1845.

†† Monthly Journ. of Med. Science. 1843, p. 1.

‡‡ De quantitate acidi carb. ab homine sano et ægroto exhalati. Havniæ, 1845.

§§ Journ. f. pr. Ch. Bd. 33, S. 120, and Bd. 37, S. 1.

|||| Ann. de Chim. et de Phys. T. 11, p. 433.

¶¶ Compt. rend. T. 20, p. 794-798, and Ann. de Chim. et de Phys. T. 11, p. 433.

*** Comment. inaug. de respir. nitrog. oxydul. Marburgi, 1844.

††† Vers. über Perspiration mit Lungen athmender Thiere. Bern. 1846.

‡‡‡ Journ. de Chim. méd. 3 Sér. T. 2, p. 477, et 751.

§§§ Compt. rend. T. 16, p. 17, and Ann. de Chim. et de Phys. 3 Sér. T. 27, p. 32 ; also Recherches chimiques de la respiration des animaux des diverses classes. Paris, 1849.

the facts relating to the respiratory process, which we now proceed to consider.

Before we pass to the subject itself, we are led to notice some of the difficulties which attended these enquiries. It is extremely difficult to procure the special materials for our investigation (the expired air) in a state of purity in sufficient quantity, and under perfectly normal conditions. Hence various methods were adopted to obtain the products of expiration, but the only mode by which the expired air could be collected pure and unmixed with the products of perspiration, consisted in the direct application (to the mouth) of an apparatus, by means of which the expired air was conveyed to suitable receiving vessels. This was the method which was usually employed in experiments on man (Dumas, Andral and Gavarret, Valentin, Vierordt). The advantages of this method over the one we shall presently proceed to notice, consisted not merely in the exclusion of the products of perspiration, but also in enabling the observer to determine the influence which certain physical conditions of respiration exerted on the numerical relations of its products. This method is, however, attended with some disadvantages, which although sufficiently serious, can hardly be foreseen; thus, for instance, a person conscious of the nature of the experiment which is being instituted, cannot help breathing in so constrained a manner as to alter the number and depth of the inspirations, so that the normal relations of the ordinarily quiet and unconscious respiration are entirely changed. This inconvenience may, however, be completely remedied by long practice; and the brilliant results and investigations both of Valentin and Vierordt are a sufficient proof that this method does not merit the condemnation which was formerly awarded to it. The objections appertaining to it may indeed be almost perfectly obviated by careful attention to the construction of the apparatus.

The second method, which Scharling and Hannover employed on man, but which most other observers have used only in the case of animals, consisted merely in allowing a current of air constantly to pass through the apparatus in which the person or animal was placed, on whom the experiment was to be made; fresh air was thus continuously supplied, and the products of expiration carried off into a system of vessels, in which the constituents of the expired air might be absorbed, and at the same time quantitatively determined. However simple this method may at first sight appear, and however conformable it may seem to nature, it possesses many deficiencies which can only be fully understood by

those who have themselves employed it. It is altogether unsuitable for the investigation of the influence exerted by the mechanical conditions of the respiration, or for the exact determination of the relations of volume existing between the inspired and the expired air, &c. For even if the apparatus is so constructed that the animals are not compelled to take deep or frequent gasping inspirations, if the air be sufficiently changed, and if the animal be removed from all keen draughts of air, and if the apparatus itself be free from a continuous alternation in the tension of the air, &c., we are only able by this method to ascertain with accuracy the absolute quantities of the carbonic acid and aqueous vapour exhaled in given times, for the quantity of the absorbed oxygen can only be determined approximately by weighing the animal both before and after the experiment, and determining the oxygen contained in the amount of exhaled carbonic acid and water, &c. The introduction of perfectly dry air, which is indispensable even to the moderate accuracy of the experiment, causes the animals to lose more water than under ordinary circumstances in consequence of their breathing in an atmosphere to which they are unaccustomed, and hence they speedily fall into an abnormal condition. The admirable investigations which Marchand has made by this method on the respiration of frogs, indicate, however, that it is capable of leading to results of the highest value to science.

A third method was employed, first by Valentin, and subsequently by von Erlach under his guidance; animals were introduced into an inclosed space filled with atmospheric air, and they were suffered to respire there for some time, when the volume and the composition of the expired air were compared with those of the original atmosphere. As far as this object is concerned, the above method gives highly satisfactory results, as may be seen from the investigations of the above-named chemists; although, as is obvious, it cannot be employed for absolute determinations, or for the investigation of the influence exerted by mechanical and physiological relations on the respiration.

An apparatus has lately been ingeniously contrived by Regnault and Reiset, by which the second and third of these methods have to some extent been combined together. The animals here also breathe in a circumscribed space, from which the carbonic acid and a portion of the expired water are constantly being removed by a solution of potash, whilst a quantity of oxygen corresponding with the amount absorbed is continuously being supplied from another vessel, without the pressure of the air being on that account sub-

jected to any considerable fluctuations. Although the advantages of this method are striking, it is not entirely free from objections, for the saturation with aqueous vapour of the air which the animal is inspiring, and the increased amount of nitrogen in the air after the long-continued respiration of animals within a limited space, are elements which must speedily exert some influence on the respiratory process.

When we pass in review the most general results yielded by different investigations on the interchange of gases in the lungs, we find in the first place, that the blood in the lungs gives off carbonic acid and aqueous vapour to the inspired air, and takes up oxygen from the latter; a very small quantity of nitrogen also commonly passes from the blood into the respired air, although under special conditions, the opposite sometimes occurs. The first question which presses itself upon our notice is undoubtedly the determination of the relation existing between the exhaled carbonic acid and the oxygen from the inspired air which has disappeared in the lungs. It is well known that the volume of carbonic acid gas is equal to the volume of the oxygen contained in it; if, therefore, a volume of carbonic acid were found in the expired air, which was equal to that of the oxygen which had disappeared from the inspired air, we might be led to conclude with many of the older inquirers, that the oxygen absorbed in the pulmonary vesicles is exactly sufficient to form the carbonic acid which they exhaled. This, however, is by no means the case, for under ordinary relations, the volume of oxygen absorbed is much larger than the volume of carbonic acid which is exhaled. The oxygen does not therefore serve merely for the oxidation of the carbon, but also for that of the hydrogen of the animal constituents. If, for instance, animals be allowed to breathe in an inclosed space, and we then analyse the air which has been modified by their respiration, we find that more free oxygen has disappeared than could have been employed in the formation of the carbonic acid contained therein; we obtain the same result if, as was done by Marchand, we compare the loss of weight in the animal during the period of the experiment, with the oxygen contained in the expired air, and distributed in the carbonic acid and aqueous vapour; for in this case we find that the animal has lost less in weight than might be expected from the quantities of excreted carbon and hydrogen; consequently a substance appreciable by weight must be absorbed by the body of the animal during respiration, and this can be no other than oxygen, as the quantities

of the nitrogen, which is either absorbed or given off, are on the whole too small to exert any special influence on this relation. Very numerous experiments have been made on this subject with all the best appliances of science. The individual results yielded by these investigations will engage our attention at a future page, and we would here only observe, that on an average for every 1 volume of absorbed oxygen, there is only about 0·8516 of a volume of carbonic acid in the expired air. We shall presently see, on comparing the investigations of modern experimentalists, that this relation appears to be a somewhat variable one, while the experiments of Brunner and Valentin, and of von Erlach, give almost exactly this proportion between the gases. According to Valentin, the interchange of these gases (corresponding to the law of their diffusion) stands in an inverse ratio to the square roots of their densities.

Attempts have frequently been made to compare the *volume* of the expired with that of the inspired air. On examining both kinds of air when freed from water, we naturally find a diminution of the volume of air, corresponding to the volume of oxygen which has been absorbed and not converted into carbonic acid. (We must, however, here disregard the small quantity of exhaled nitrogen.) The result will certainly be different when both kinds of air are compared together in a moist state; since the inspired air is usually not saturated with aqueous vapour, while the reverse is the case with the expired air, it necessarily follows that the tension of the aqueous vapour taken up in the lungs must cause an increase in the total volume of the air.

We need scarcely observe that the elevation of temperature which the air commonly experiences in respiration, (from 36·2 to 37·5°, according to Valentin,) must occasion a corresponding augmentation of volume.

The quantity of *water* exhaled by an adult man in a state of rest in 24 hours amounts, according to Valentin, to 506, according to Vierordt to 360, and according to Horn to 350 grammes; as, however, aqueous air was inspired in the experiments of the last-named observers, the actual loss of water is only 321 grammes.

We have already shown, that the *quantity of nitrogen* in the air does not remain precisely the same during respiration. Various views were long entertained in reference to the question, whether nitrogen gas was absorbed or exhaled during respiration; the more modern investigations of Brunner and Valentin, as well as those of Regnault and Reiset, have now placed it beyond a doubt that

there is an excretion of nitrogen, although only in extremely small quantity. According to the former of these inquirers, the expired air was about 0·402% (by volume) richer in nitrogen than the inspired air; whilst the latter observers found in their experiments on animals, that for every 10,000 parts by weight of absorbed oxygen, from 8 to 133 parts of nitrogen were developed in the lungs. Boussingault* had already endeavoured at an earlier period to prove this fact by an indirect method, namely, by comparing the quantity of nitrogen taken into the system with the food, with that contained in the fluid and solid excrements, and the result was, that the quantity of nitrogen present in the excrements was below the amount taken up with the food, and hence it was concluded that the deficient quantity of nitrogen must have been excreted from the organism through the lungs. Boussingault found that the relative weights of the exhaled nitrogen and the expired carbonic acid were nearly as 1 : 100. Barral† obtained the same result in his experiments on men, for according to him the quantity of exhaled nitrogen amounts to about 1-100th of the quantity of the excreted carbonic acid. We have already observed (in vol. i, p. 453) that a portion of the nitrogen occurs in the expired air under the form of ammonia.

In addition to these very slight traces of ammonia, the expired air not unfrequently also contains volatile substances which have been taken with the food, such as alcohol, phosphorus, camphor, and ethereal oils; and even when no such substances can be detected in the food, small quantities of an organic carbohydrogen are found in the expired air. The reddening which sulphuric acid undergoes when used for the purpose of drying the expired air also indicates this fact; but when, as in most experiments on animals, certain products of perspiration are intermixed with the expired air, this coloration may depend upon the gases of the intestinal exhalations, or in case the second of the methods above indicated have been employed, it may be owing to the presence of mechanically adhering organic parts, as, for instance, dust from the skin of the animal. But even where respired air, in which no impurities are present has been employed, a slight colouring of the acid may be constantly observed after the air has been suffered to pass uninterruptedly through a sulphuric acid apparatus. It seems tolerably well established, from the very exact

* Ann. de Chim. et de Phys. 2 Sér. T. 61, p. 128; and 3 Sér. T. 11, p. 433, and T. 12, p. 153.

† Compt. rend. T. 27, p. 361.

experiments of Regnault and Reiset, that the hydrogen and the carburetted hydrogen which they found in air which had served for a prolonged time for the respiration of animals, were not dependent solely upon the perspiration or the intestinal exhalation, but that an appreciable quantity both of hydrogen and proto-carburetted hydrogen was exhaled from the lungs when in a perfectly normal condition.

We will now proceed to establish several *absolute values* which the above-named investigators have obtained in reference to many of these points. We possess very different statements regarding the quantity of *carbonic acid* exhaled within a definite time by an adult man. The cause of this diversity may readily be comprehended, when we consider the methods by which these numbers have been obtained. With the exception of Scharling and Vierordt, all other observers have contented themselves with collecting the air of only a few respirations, and, after determining the amount of carbonic acid, have calculated the quantity of this gas for a definite period of time. We have already seen how easily we may be led into error, from want of practice, by the determination of individual respirations, and these errors augment in proportion to the length of time (as, for instance, 1 hour or 24 hours) for which we endeavour to establish the exhalation of carbonic acid. We will therefore pass over the older results, which vary considerably, merely observing that, according to Scharling, a very powerful adult man exhales in 24 hours 867 grammes, or at a temperature of 0°, and the barometer at 336‴ [29·84 inches,] 443,409 cubic centimetres [or about 27,058 cubic inches] of carbonic acid. Basing his calculations on Valentin's law, Vierordt therefore calculates that the amount of oxygen absorbed by an adult in 24 hours (and partly given off again with the carbonic acid and the water, and partly remaining in the body) amounts to 746 grammes, or 520,601 cubic centimetres [or about 31,740 cubic inches]; consequently about 116 grammes of the *absorbed oxygen* are retained in the organism. According to Boussingault's determinations, about 8 grammes of nitrogen would be given off to the atmosphere in the same period of time by the same individual, whilst, according to Valentin, about 500 grammes of water are exhaled on an average in equal intervals of time. The numerous and carefully conducted experiments of Vierordt show that the air exhaled by a healthy man in a state of rest contains on an average 4·334% by volume of carbonic acid.

The above remarks indicate that the frequency or depth of the respiratory movements must exert considerable influence on the interchange of gases in the lungs. Before we proceed to the other relations by which the pulmonary functions are modified, we will consider these purely mechanical relations somewhat more attentively, especially since many other physical and physiological influences affect the respiratory functions, and particularly the excretion of carbonic acid, only in an indirect manner by modifying the respiratory movements. Notwithstanding the attention which has been directed to the mechanism of respiration in its anatomical and physiological relations, and the number and excellence of the investigations made in reference to the chemical constitution of the expired air and the differences which it presents under the most different physiological conditions, this most important factor in the process of respiration remained almost entirely unnoticed until Vierordt published his well-known work on the subject, which he has so thoroughly exhausted that all our knowledge of the relations in question may in fact be referred to him alone. We cannot, therefore, do better than follow him as our guide in these inquiries.

Vierordt first limited his investigations solely to the determination of the dependence of the amount of carbonic acid in the expired air upon the *frequency of the respiratory movements*; to ascertain this relation, he began by observing the quantities of carbonic acid excreted during perfectly quiet respiration, in order to obtain certain mean values and to establish the corresponding variations. All Vierordt's experiments were made upon himself, and, as nearly as possible, under the same conditions. The duration of each experiment was limited to a minute, and the air collected during that period was tested for its amount of carbonic acid. Before each experiment a few respirations were made, corresponding in frequency as nearly as possible to those made during the period of the experiment, since the air remaining in the lungs from the previous respirations might have induced a relative error in the result of the observation. These comparative observations on the different frequency of the respiration were not made consecutively, but at intervals of about half an hour, and, as far as possible, at the same time of the day. The volumes of gases given in the following table are calculated for a temperature of 37°, and the barometer at 336 Paris lines.

Vierordt found the following mean values, to which we add the

maxima and minima, for the respiratory function for one minute during a state of perfect bodily repose.

	Mean.	Minimum.	Maximum.
Number of pulsations	75·52	54	101
„ respirations	11·9	9	15
Volume of the expired air	6034·0 c. c.	4206·0 c. c.	9331·0 c. c.
	[or 384·7 c. i.]	[or 256·6 c. i.]	[or 568·2 c. i.]
„ expired carbonic acid	261·52 c. c.	177·0 c. c.	452·0 c. c.
	[or 16·00 c. i.]	[or 10·8 c. i.]	[or 27·6 c. i.]
„ of one expiration	507·0 c. c.	367·0 c. c.	699·0 c. c.
	[or 31·0 c. i.]	[or 22·4 c. i.]	[or 42·7 c. i.]
Carbonic acid in 100 parts of expired air	4·334	3·358	6·220

After having obtained these fundamental values, Vierordt tried the experiment of breathing with double the rapidity without diminishing the normal depth of the inspiration, and he then obtained the result that the relative quantity of carbonic acid was on an average about 0·907$\frac{0}{0}$ less than in normal undisturbed respiration; when the number of inspirations were increased three times their former amount this diminution was about 1·125$\frac{0}{0}$; when the number was increased fourfold it was 1·292$\frac{0}{0}$; and finally, when they were increased eightfold it was about 1·600$\frac{0}{0}$. When the number of the inspirations was diminished by one-half, (when only 6 instead of 12 inspirations were made in a minute, which occasioned considerable difficulty of breathing, and hence could not yield a perfectly pure result,) the difference in the quantity of carbonic acid in the expired air was found to be 1·316$\frac{0}{0}$. This relation will be rendered more clear by the following comprehensive arrangement of mean values found by Vierordt, in which the mean quantities of the carbonic acid obtained during respirations of different rapidity, are calculated for one and the same normal quantity of carbonic acid.

Acts of respiration in one minute.	Carbonic acid in 100 vols. of expired air.
6	5·528
12	4·262
24	3·355
48	2·984
96	2·662

Vierordt was able, after a few corrections made in the numbers thus obtained, to show that the numbers of the respirations are

functions of the numbers expressing the corresponding per-centage of carbonic acid. Thus for every expiration, without reference to duration, there is a constant amount of carbonic acid (of $2{\cdot}5\frac{0}{0}$), to which we must add a second value expressing the quantity of carbonic acid exactly proportional to the duration of the respiration. We subjoin the following table in elucidation of this proposition:

Respirations.	Per-centage of carbonic acid.	Constants.	Augmentation of the per-centage of the carbonic acid for the duration of the respiration.
6	5·7	2·5	3·2
12	4·1	2·5	1·6
24	3·3	2·5	0·8
48	2·9	2·5	0·4
96	2·7	2·5	0·2

[The author here quotes Vierordt's formula, representing (as that chemist believes) the connexion between the per-centage of the carbonic acid and the number of respirations in a minute. As, however, it would not be intelligible to the general reader without a much fuller explanation than is given in the original text, we deem it advisable to omit it.—G. E. D.]

Stürmer,* who carried on a series of investigations on this subject under the direction of Marchand, obtained somewhat different results from those of Vierordt, although upon the whole they arrived at tolerably similar conclusions. As Stürmer and Marchand's results did not, however, admit of being expressed by Vierordt's formula, they attempted in some degree to modify it. Several objections were advanced against Vierordt's method, as, for instance, the expiration into the expirator with open nostrils, the employment of a solution of common salt as a separating fluid, and the neglect of the difference of the tension of its vapour from that of pure water, the inaccurate determination of the temperature of the air in the anthracometer, and the uncertainty in the reading of the water-line, &c. Most of these objections were, however, recognised and specified by Vierordt himself, and we agree with him in thinking that they do not materially influence the main results; for although we by no means hold the view that a very large number of less exact experiments are able to give a better result than a few very accurate observations, (since, if this were the case, an astronomer might as well content himself with

* Observ. de acidi carbonici respiratione exhalati quantitate. Halis, 1848.

taking the mean of the times of 100 clocks instead of employing one costly but reliable chronometer,) Vierordt's experiments appear to us fully to merit the confidence which their author himself places in them. One of the most essential requirements towards the success of such experiments undoubtedly consists in the power of carrying on the normal respirations in a quick and undisturbed manner, and in this respect Vierordt has a decided advantage over Stürmer. The latter observer obtained the following mean quantities from eight or ten experiments with the expired air.

6 Respiratory movements in the minute	yielded	5·45	per cent.	of carbonic acid.
12 "	"	4·57	"	"
24 "	"	3·50	"	"
48 "	"	2·65	"	"

According to Vierordt's experiments, 500 cubic centimetres [or 30·5 cubic inches] are about the mean value for the volume of the air expelled by one expiration when the breathing is undisturbed. If now we assume, during hurried respiration, an equally large volume for the air expelled by each expiration, the absolute amount of carbonic acid exhaled in a minute may be very readily calculated from the above data. The following table plainly shows the relations deduced from this calculation.

Number of expirations in one minute.	Carbonic acid in 100 volumes of expired air.	The quantity of air expired in one minute.	The quantity of carbonic acid expired in one minute.	The carbonic acid exhaled in one expiration.
6	5·7	3,000 c. c. [or 183 c. i.]	171 c. c. [or 10·4 c. i.]	8·5 c. c. [or 1·7 c. i.]
12	4·1	6,000 c. c. [or 366 c. i.]	261 c. c. [or 13·5 c. i.]	20·5 c. c. [or 1·3 c. i.]
24	3·3	12,000 c. c. [or 733 c. i.]	396 c. c. [or 24·2 c. i.]	16·5 c. c. [or 1·0 c. i.]
48	2·9	24,000 c. c. [or 1,463 c. i.]	696 c. c. [or 42·5 c. i.]	14·5 c. c. [or 0·88 c. i.]
96	2·7	48,000 c. c. [or 2,928 c. i.]	1,296 c. c. [or 79 c. i.]	13·5 c. c. [or 0·82 c. i.]

Vierordt subjoins some interesting remarks on the number of respirations which must be made in a minute in order to remove the whole of the carbonic acid from the blood circulating through the lungs. If, for instance, we assume with him that the quantity of carbonic acid in the blood passing in one minute through the pulmonary capillaries amounts to 4300 c. c. [or 262 cubic inches], it would require, according to the above data, upwards of 300 respiratory acts for its entire removal; for 192 respirations would only remove 2496 c. c. [or 152 cubic inches], whilst twice that number might separate as much as 4896 c. c. [or 299 cubic inches,] supposing that such excessive frequency of

respiration were within the limits of possibility. In accordance, however, with his view of the quantity of carbonic acid contained in the blood of the pulmonary capillaries, six respirations within the minute would expel only 3·97$^0/_0$ of carbonic acid; twelve would yield 5·72$^0/_0$; twenty-four 9·21$^0/_0$; and forty-eight 16·18$^0/_0$.

Although several causes, besides the frequency of respiration, exert the most marked influence on the quantity of carbonic acid in the expired air, this law nevertheless remains in force for otherwise similar conditions, as Vierordt has convinced himself by numerous series of experiments instituted under the most various bodily conditions. We must, therefore, assume with him, that the rhythm of the respiration acts as the most powerful regulator of the excretion of carbonic acid.

The influence of the respiratory movements on the excretion of carbonic acid is equally manifested, when we consider the *intensity or depth of the individual respirations.* Notwithstanding the difficulty of drawing respirations of a certain depth, Vierordt has been able to obtain very decisive results in relation to this point, as may be seen in the following table:

If the air of normal respirations contain		4·60	per cent.	of carbonic acid,
The air in respirations twice as deep contains		4·00	„	„
three times	„	3·70	„	„
four times	„	3·38	„	„
eight times	„	2·78	„	„
half	„	5·38	„	„

From these observations it follows, that in an expiration having double the normal volume, the absolute quantity of the exhaled carbonic acid is about equal to that which is exhaled by respirations having threefold the normal frequency; whence it is further proved that the organism possesses two means of at the same time separating larger quantities of carbonic acid.

Vierordt adopted two methods of determining the question, whether the amount of carbonic acid in the air increases in the finer ramifications of the air-passages, as the experiments of Allen and Pepys, and of Jurine, seem to show. One method consisted in dividing each expiration into two as nearly as possible equal parts; the expired air in the latter half must have arisen from the deeper parts of the lungs, and Vierordt found in it 5·44$^0/_0$ of carbonic acid as the mean of 21 experiments, whilst the first half contained on an average only 3·72$^0/_0$. The other method consisted in comparing the amount of carbonic acid in a normal expiration with that in the air obtained by an intensely forced expiration. He found as the

mean result of eight experiments, that while the carbonic acid of a normal expiration (of 574 c. c.) amounted to 4·63%, a most complete and full expiration (of 1800 c. c.) contained 5·18%. Hence it follows that in the deeper strata (amounting to 1226 c. c.) of the strong expiration, (the quantities contained in both expirations amounting to 26·57 and 93·34 c. c. respectively,) there are 66·67 c. c. (or 5·43%) of carbonic acid, and consequently 0·80% more than the amount contained in the volume of a normal expiration. As, however, there always remain about 600 c. c. of air in the lowest parts of the lungs even after the strongest expiration, the highest per-centage amount of carbonic acid in the air in the pulmonary cells would be about 5·83%, that is, 1·2% more than is contained in the air of a normal expiration.

Vierordt made four series of experiments on the influence which *obstruction* of the respiration exerts on the secretion of carbonic acid. All these experiments generally exhibited a very considerable decrease in the absolute amount of carbonic acid, and a considerable increase in its relative amount—a result to which Horn* has also been recently led in a series of analogous experiments.

We now proceed to the consideration of those changes which the expired air experiences from the indirect action of chemical agents, that is to say, more especially from the *inhalation of artificial atmospheres, or of different kinds of gases.* The latest experiments of Regnault and Reiset, on dogs and rabbits, show that the respiration of air which is richer in oxygen than the atmosphere, does not produce effects differing from those yielded under the normal relations; the animals did not exhibit any distress from the inhalation of air containing two or three times more oxygen than our atmosphere, and the products of respiration were precisely the same as when the animals had breathed atmospheric air. It is therefore the more striking, that the earlier experiments on respiration in pure oxygen should have led to tolerably decisive results; among these we must include the observations of Lavoisier and Seguin, as well as those of Allen and Pepys on man, and those of Marchand on frogs. According to these observers, the excretion of carbonic acid was only very slightly or not at all increased by breathing in pure oxygen, although far more oxygen was absorbed than under ordinary conditions. According to Marchand, for instance, there remained

* Neue medic.-chirurg. Zeitung. 1849, S. 33-39.

more oxygen in the blood (which was not expended in the formation of carbonic acid) than in respiration in ordinary air. The experiments of Allen and Pepys exhibit, moreover, no inconsiderable exhalation of nitrogen. Sir Humphrey Davy's experiments (according to which most of the vital functions are performed with augmented energy after the prolonged inhalation of oxygen) are worthy of being carefully repeated with such improved means as Lespasse* has lately employed in his observations.

The respiration of air *richer in carbonic acid* than the ordinary atmosphere, and the repeated inspiration of air which had already been expired, have been made the subject of numerous investigations. Marchand found that frogs which had been suffered to breathe in closed vessels, developed less carbonic acid and inhaled less oxygen towards the close of the experiments than at the beginning, and that at length they absorbed little more oxygen than was necessary for the formation of carbonic acid. The experiments made by Legallois† on animals, present results differing so essentially from those obtained by other observers, that one scarcely knows how far to trust them. The following fact seem, however, to possess some degree of probability. A larger amount of nitrogen is excreted in an atmosphere rich in carbonic acid than in the ordinary air, and when the air is very richly charged with carbonic acid some of this substance is even absorbed by the blood; the absorption of oxygen is in that case proportionally small.

Davy's experiments prove that pure carbonic acid cannot be inhaled, as the glottis spasmodically obstructs its passage; 60 or even 40% of carbonic acid are sufficient to render an atmosphere unfit for respiration, although air less densely charged with this acid may be respired for some time without producing any injurious effects, and the danger induced by its prolonged respiration depends less upon the actual amount of carbonic acid than upon the insufficient supply of oxygen conveyed to the lungs by such an atmosphere.

It has been shown by Legallois' experiments on guinea pigs, that in air which is *richer in nitrogen* than the atmosphere, nitrogen is absorbed and less carbonic acid exhaled; the absorption of oxygen appears to be relatively greater than in atmospheric air.

The inhalation of pure nitrogen gas is speedily followed by

* Compt. rend. T. 22, p. 1055.

† Exp. sur le principe de la vie. Paris, 1812.

symptoms of suffocation; according to Coutenceau* and Nysten,† rather more carbonic acid appears to be exhaled than in the atmospheric air.

The most careful experiments have been made on the respiration of *nitrous oxide* by its discoverer, Humphrey Davy, and these observations have been perfectly corroborated in recent times by Ph. Zimmermann.‡ The first effects are manifested by pleasurable sensations, considerable excitement, and a state resembling intoxication, but this speedily (after the lapse of five or ten minutes) passes into asphyxia. According to Davy's analyses of the expired air, a large quantity of nitrous oxide is absorbed by the blood; carbonic acid and nitrogen being given off in no larger quantities than usual. Zimmermann made numerous experiments with this gas on pigeons and rabbits, and found that the pulse soon became irregularly quickened, and the respiration very frequent, these symptoms being followed after a time by slight convulsions and asphyxia. A strong rabbit was resuscitated by the artificial inhalation of atmospheric air, after the animal had remained for 3 hours and 20 minutes in an atmosphere of nitrous oxide. Zimmermann found that a rabbit which yielded on an average 0·8 of a gramme of carbonic acid in atmospheric air, exhaled 1·3 grammes, when respiring nitrous oxide.

Respiration may be carried on without injury for a tolerably protracted period in an atmosphere containing *hydrogen gas*, if a sufficient quantity of oxygen be present. Regnault and Reiset caused rabbits, a dog, and frogs to respire in an atmosphere whose nitrogen had been for the most part replaced by hydrogen (from 55 to 77% of hydrogen, from 1·1 to 14·4% of nitrogen, and from 21·8 to 28·8% oxygen); the rabbit remained in this atmosphere 20 hours and the dog 10 hours without any obvious injury, excepting that the respiration was augmented in force—a circumstance which these observers thought they might refer to the greater cooling power of the hydrogen. At the close of the experiment nearly the original amount of hydrogen was found; there was a more considerable absorption of oxygen than in the case of atmospheric air. Nitrogen appeared to be exhaled; but this might have been derived from the air already in the lungs of the animals, when they were introduced into the apparatus in which they were made to respire. The respiration of these animals pro-

* Révision des nouv. doctr. chem.-physiol, &c. Paris, 1814.

† Recherches de Physiol. et de Chim. pathol. Paris, 1811.

‡ Diss. inaug. med. Marburgi, 1844.

ceeded, therefore, quite as regularly in this artificial atmosphere as in ordinary air—a circumstance which had already been observed by Lavoisier and Seguin, as well as by Humphrey Davy.

It is clearly shown by Regnault and Reiset's experiments that the only reason why respiration cannot be supported for any length of time in pure hydrogen gas is, that the organism is thus deprived of the oxygen necessary for life. Marchand found that frogs died in from half-an-hour to an hour after being placed in pure hydrogen gas; they exhaled a much larger quantity of carbonic acid in this gas than in atmospheric air, for whilst 1000 grammes' weight of frogs exhaled about 0·077 of a gramme of carbonic acid in one hour in atmospheric air, they developed as much as 0·263 of a gramme of carbonic acid in the same time in pure hydrogen gas.

Carbonic oxide gas, when mixed even in very minute quantities with atmospheric air, gives rise to faintness, feelings of suffocation, stupefaction and death. The fact of this being the constituent to which choke-damp owes its fatal effects, has been especially demonstrated in recent times by Leblanc.*

We need hardly observe that sulphuretted hydrogen, seleniuretted hydrogen, phosphuretted hydrogen, arseniuretted hydrogen, ammoniacal gas, sulphurous acid, chlorine, &c., are not merely irrespirable, but are also poisonous gases, like carbonic oxide.

Like all the other functions of the animal organism, the respiration is acted upon in a definite manner by numerous influences of the external world. The animal body is brought into the most intimate relation with the atmosphere through the medium of the lungs; and hence the effects of various atmospheric conditions are discernible in the different respiratory functions. In consequence of these relations, we will investigate the alterations apparent in the composition of the expired air during different conditions of the atmosphere; amongst which the *temperature* first claims our attention. The earliest experiments made in relation to this point were for the most part limited to those animals which at low temperatures either fall into a state resembling hybernation, or whose vital activity is at all events more or less reduced. As Spallanzani, Saissy, Treviranus, and others had observed that insects and molluscs, as well as marmots, bats, and hedgehogs, exhaled less carbonic acid in a low than in a high temperature, it was at once assumed as a general proposition, that

* Compt. rend. T. 30, p. 483.

a depression of the surrounding temperature would constantly produce this effect in all classes of animals. The numerous and variously modified experiments which have since been made in connection with this inquiry have, however, proved that in the higher classes of animals at all events there is a diminution in the exhalation of carbonic acid corresponding with the rise of the temperature from the freezing point. Letellier* was one of the first of several observers who in recent times have made a series of determinations of the quantities of carbonic acid exhaled by different animals, as green-finches, turtle-doves, mice, and guinea-pigs, at various lower or higher temperatures. His results showed that the largest relative amount of carbonic acid was exhaled in a temperature between -5° and $+3^\circ$, and the smallest at a temperature between $+28^\circ$ and 43°. This ratio is more strongly marked in birds than in the mammals; the animals on which these experiments were made were unable to bear a temperature exceeding $+43^\circ$. Almost simultaneously with Letellier, Marchand obtained similar results with frogs; with this difference only, that these animals already fell into a torpid state between $+2^\circ$ and 3°, in which they excreted a remarkably small amount of carbonic acid, 1000 grammes' weight of frogs yielding only 0·039 of a gramme in one hour, whilst the largest amount was exhaled between 6° and 7°, 1000 grammes' weight yielding 0·124 of a gramme; the quantity of excreted carbonic acid then gradually sunk in proportion to the rise of the temperature. Between 28° and 30°, 1000 grammes' weight of frogs exhaled only 0·077 of a gramme in one hour.

Vierordt has calculated a scale of the values of the respiratory functions, according to each degree of temperature between 3° and 24°, basing his numbers on the results of his numerous experiments on the excretion of carbonic acid, in which he noted the thermometric and barometric readings, as well as the pulsations and respirations, and the volumes of the individual expirations throughout the entire experiment. These tables afford a better insight into the influence of the temperature on the respiration than we obtain from any of the earlier observations on the same subject. For the better comprehension of these relations, we divide the mean result into two sections, of which the one represents the means of the values obtained in the lower degrees of temperature between $+3^\circ$ and 13°, and the other those between 14° and 24°.

* Compt. rend. T. 20, p. 794.

	Average Temperature. 8·47°	Average Temperature. 19·40°	Difference.
Pulsations in one minute....	72·93	71·29	1·64
Respirations in one minute	12·16	11·57	0·59
Volume of one expiration .	548·0 c. c. [or 33·5 c. i.]	520·8 c. c. [or 31·8 c. i.]	27·2 c. c. [or 1·7 c. i.]
Air expired in one minute .	6672·0 c. c. [or 407·0 c. i.]	6106·0 c. c. [or 367·2 c. i.]	656·0 c. c. [or 40·0 c. i.]
Carbonic acid in one minute	299·33 c. c. [or 18·3 c. i.]	257·81 c. c. [or 15·70 c. i.]	41·52 c. c. [or 2·60 c. i.]
Carbonic acid in 100 parts of expired air	4·48	4·28	0·20
State of the barometer	334·60 Paris lines [or 29·73 inches].	333·82 Paris lines [or 29·64 inches].	

This table not only shows that the number and depth (volume) of the respirations decrease with the elevation of the temperature, but it also exhibits the indirect influence of temperature on the excretion of carbonic acid, from its absolute quantity being considerably diminished by the diminution of the number and extent of the expirations; in the meanwhile the per-centage amount of this gas in the expired air is also decreased; whence the elevation of the temperature must necessarily influence the excretion of carbonic acid by some other means than by diminishing the mechanical functions of respiration.

Vierordt has also determined similar relations in regard to the quantities of water expired at different temperatures,* as may be best seen in the following table:

Temperature of the air.	Inspired air reduced to the corresponding temperature, and 336‴ B.	Expired air reduced to 37° and 336‴ B.	Water expired in one minute, in grammes.	Quantity of water in the air inspired in one minute, in grammes. Perfectly saturated.	Quantity of water in the air inspired in one minute, in grammes. With the mean amount of water.	Loss of water in the body in one minute, in grammes. When breathing saturated air.	Loss of water in the body in one minute, in grammes. When breathing air, containing the mean amount of water.
4°	5827	6634	0·27988	0·03997	0·02435	0·23991	0·25553
9°	5680	6334	0·26723	0·05219	0·02471	0·21503	0·24251
14°	5522	6034	0·25454	0·06760	0·02772	0·18696	0·22685
19°	5253	5734	0·24191	0·08682	0·03725	0·15509	0·20466
24°	5234	5430	0·22926	0·11164	0·04156	0·11461	0·18770

The degree of moisture of the atmosphere is not without influence on the respiratory functions, and especially on the excretion

* Abhandl. bei Begründung der k. sächs. Ges. d. Wiss. Leipzig, 1846.

of carbonic acid. I have made several experiments in reference to this subject on wood-pigeons, green-finches, and rabbits. The weight of carbonic acid excreted in moist air greatly exceeds that eliminated in a dry atmosphere; thus, for instance, 1000 grammes' weight of male wood-pigeons yielded in one hour in the morning in a *dry* air 10·438 grammes of carbonic acid at 0°, 6·055 grammes at 24°, and 4·69 grammes at 37°; in a *moist* atmosphere they yielded 6·769 grammes at 23°, and 7·76 grammes at 37°.

In the same way 1000 grammes' weight of green-finches yielded in the course of one hour in the afternoon in *dry* air 7·260 grammes at 0°, 5·679 grammes at 17·5°, and 3·220 grammes at 37·5°. In *moist* air they yielded 5·351 grammes at 17·5°, and 6·851 grammes at 37·5°. Lastly, 1000 grammes' weight of rabbits exhaled in one hour before noon 0·451 of a gramme of carbonic acid in *dry* air at a temperature of 37·5°, and as much as 0·677 of a gramme in a *moist* atmosphere at the same temperature.

Few as these investigations are, they yet clearly demonstrate the importance of this influence on respiration, which we have frequently had opportunities of observing at the bed-side, more especially in the case of pulmonary diseases. It is only when we proceed to inquire into the causal connection existing between the excretion of carbonic acid which is here observed, and the degree of moisture of the inspired air, that we are compelled to admit our insufficient knowledge of this subject.

The influence exerted by the moisture of the air on the respiratory movements is not a question of mere conjecture, since it admits of direct observation. The respirations of animals are more frequent in a moist warm atmosphere than in a dry one; but this result depends very much upon the change to which the animals are subjected at the beginning of the experiment; but when the frequency of the respiration is observed, 3, 6, or 10 hours after the commencement of the experiment, it is always found to be more considerable than in a dry atmosphere. It appears, however, from some experiments made by Buchheim in my laboratory, that the moisture of the air even more decidedly influences the depth of the inspirations. But although the augmentation in the expired carbonic acid, when breathing in a moist air, may be partially explained by the alteration in the respiratory movements to which we have already referred, the influence of moisture, like that of the temperature, probably also acts in some other way. Our knowledge of these relations does not as yet enable us to prove that the aqueous vapour exerts any direct influence on the excretion of carbonic acid from the blood. I have repeatedly made an obser-

vation in reference to this subject, which may, I think, prove of some interest towards the further elucidation of this question. I have found that frogs lose much less of their weight in a dry than in a moist atmosphere, the difference being very considerable. The two following of my numerous observations may suffice to demonstrate this difference. In one case 100 grammes' weight of frogs lost 1·820 grammes of their weight in twenty-four hours in a dry atmosphere, and as much as 4·376 grammes during the same period of time in moist air; in another experiment they lost 0·681 of a gramme in dry, and 5·340 grammes in moist air. It is very obvious that these conditions depend chiefly upon the perspiration, and do not, therefore, present a perfectly parallel case with the respiration of the higher animals; for the external appearance of the frogs which were in the dry air, showed that their skin was dry, and consequently in an unfit state for carrying on the process of respiration; but still this observation may not be entirely unconnected with these respiratory conditions. It also shows the necessity for practising caution in drawing our conclusions from experiments made on animals which have only respired a perfectly dry air. We cannot possibly observe normal conditions of respiration in experiments conducted merely in dry air, although this one element may not be of great importance in reference to the consideration of the whole process.

The *pressure of the air* is another of the atmospheric influences which reacts upon the respiration. We will here first refer to the most recent experiments made in relation to this subject, partly because they are limited to respiration in the human organism, and partly because they have led to the adoption of far more correct views regarding the influence of atmospheric pressure than could be obtained from the earlier observations on animals. Here too we are mainly indebted to Vierordt for our knowledge. His numerous experiments at different heights of the barometer yield the following values for the individual functions of respiration.

Height of Barometer.	Pulse.	Volume of one Expiration.	Amount expired in one minute of		Relative amount of carbonic acid.
			Air.	Carbonic acid.	
332·04 Paris lines [or 29·48 inches].	70·9	528·9 c.c.	6121 c. c.	272·51 c. c.	4·450 per cent.
337·71 Paris lines [or 29·79 inches].	72·2	529·2 „	6607 „	271·16 „	4·141 per cent.

A rise in the barometer of 5·67‴ therefore increases the pulsations 1·3, the respirations about 0·74, and the amount of expired air 586 c. c. [or 35·7 cubic inches] in a minute, whilst the carbonic acid of the latter sinks about 0·309%. Vierordt further remarks that these differences are made more apparent when respiration is carried on at higher temperatures.

Legallois placed dogs, cats, rabbits, and guinea-pigs in an atmosphere which was only one-third as dense as the ordinary atmosphere, and compared the results of these experiments with others obtained from observations conducted at the ordinary pressure of the atmospheric air. We cannot, however, attach any great value to these experiments, because the sudden change in the atmospheric pressure must necessarily have disturbed the other functions of these animals to so great a degree as essentially to vitiate the purity of the observation. Although my own experiments on rabbits and green-finches, in connection with this point, are not free from all grounds of objection, I have endeavoured, as far as possible, to distinguish between the effects of the alternation in the pressure of the air, and those depending upon the constant atmospheric pressure. I found by direct observation, that every rapid change in the pressure of the air, whether this change were one of increase or diminution, gave rise to accelerated respiration both in birds and in mammals, and, consequently, that it was connected with increased exhalation of carbonic acid. My experiments were, therefore, conducted in such a manner as to accustom the animals to an increase or diminution of the ordinary atmospheric pressure, after which the quantity of carbonic acid expired within a definite time under such an increased or diminished atmospheric pressure, was determined. The results obtained presented nearly the same degree of variability, although in some cases the pressure was raised to 34″, and in others it fell to 22″. Although, for instance, in one case 1000 grammes' weight of green-finches exhaled 5·921 grammes of carbonic acid when the barometer stood at 739 m. m., and 6·313 grammes when the barometer was at 805 m. m. the temperature in both cases being +13°, and in another case 1000 grammes' weight of rabbits exhaled 0·529 of a gramme of carbonic acid with the barometer at 704 m. m., and 0·600 grammes with the barometer at 801 m. m., the temperature in both cases being 15°, and there would, therefore, seem to be some ground for the hypothesis that an augmentation of the carbonic acid was due to increased atmospheric pressure; yet the most general result to be deduced from the tolerably accordant

experiments made in reference to this subject seem nevertheless to prove that a diminution of pressure of the air gives rise to a slight decrease in the quantity of exhaled carbonic acid, whilst an augmentation of pressure occasions a slight increase in this gas, and that the absolute pressure of the atmosphere must consequently exert a very subordinate influence on the exhalation of carbonic acid. The animals which were employed for these experiments were, however, quite as lively and as much disposed to eat with the barometer both at 34″ and at 22″ as at the mean pressure.

Marchand made several experiments on the condition of frogs, when inclosed in a space from which *the air had been almost entirely withdrawn.* When the air-pump was worked slowly, the animals began to show symptoms of uneasiness, and their bodies swelled at a pressure of 54 m. m. [21·25 inches], and at a pressure of 4 m. m. [0·16 of an inch] they exhibited considerable inertia, and many of them became asphyxiated. After remaining for even half an hour *in vacuo*, the animals recovered on a re-admission of air. If the animals were killed by complete abstraction of air, it was found that 1000 grammes' weight of frogs would eliminate about 0·600 of a gramme of carbonic acid.

Prout's experiments on the influence of the different *periods of the day* upon the exhalation of carbonic acid have been repeated by several observers, amongst others by Scharling, Vierordt, and Horn,* who have noticed that the different periods of the day occasion decidedly appreciable differences in this respect. We fully concur, however, with Scharling and Vierordt in referring these differences far more to internal conditions of the organism, such as digestion, waking and sleeping, &c., than to cosmical relations, if indeed the later claim any consideration. It would at all events appear from the experiments of these observers, that the influence of the different periods of the day, if the above physical relations be set aside, is reduced to a minimum. It must not, however, be forgotten that the numerous experiments of Bidder and Schmidt† perfectly coincide with those of Chossat‡ in showing that animals, when fasting, constantly exhale far less carbonic acid during the night than by day, this relation continuing unaltered up to the time of death. As these oscillations were found by Schmidt to cease after the animals had been blinded, they cannot be entirely owing to sleeping and waking; for although light in itself

* Op. cit.

† Op. cit., p. 317.

‡ Recherches expérim. sur l'inanition. Paris, 1843, p. 67.

may exert some influence on these corporeal conditions, it must be very indirect in its nature.

Marchand was induced to believe from his earlier experiments on frogs, that the difference between the diurnal and nocturnal excretion of carbonic acid was very considerable; he found, however, from his subsequent observations, that the apparent excess of the diurnal over the nocturnal excretion in his former experiments was entirely owing to the circumstance that the frogs were employed for the day-experiments immediately after their capture, while the same exhausted animals were again used for the night-observations. Marchand has, therefore, also been led to the conclusion, that the influences of day and night are very inconsiderable, and that the slight diminution in the excretion of carbonic acid during the night can only be referred to the more quiet condition of the animal during that time.

It might, *a priori*, be concluded that those *internal conditions of the animal organism* which are closely connected with *nutrition*, and which, therefore, have a direct bearing upon the constitution of the blood, must exert the most marked influence on the respiration; and such indeed has been proved to be the case by various experiments on the respiratory functions during digestion, as well as during fasting, and after the use of certain articles of food and drink.

On passing to the consideration of the condition of the respiration *during complete abstinence from food*, we find that all observers coincide in this point, that fasting essentially influences all the excretions, including that of the lungs. Letellier found that 1000 grammes' weight of turtle-doves, which exhaled 5·687 grammes of carbonic acid in an hour when they were fed upon grain, excreted only 4·120 grammes of this gas within the same time after having fasted seven days. Boussingault* made a similar observation on the same animals, and found that 1000 grammes' weight of them, which hourly exhaled 4·169 grammes of carbonic acid when fed with millet, yielded only 2·050 grammes after a seven days' fast. Marchand has very carefully investigated the diminution of the respiratory products and their relation to the absorbed oxygen in frogs while fasting. His numerous series of experiments, some of which embrace long intervals of time, appear clearly to show that these animals gradually exhale less carbonic acid, and absorb less oxygen; it is, however, worthy of notice that the ratio of the absorbed oxygen to the exhaled carbonic acid, always rises until it

* Ann. de Chim. et de Phys. 3 Sér. T. 11, p. 433.

reaches the proportion of about 420 : 200, when the great quantity of oxygen must necessarily be employed for the oxidation of the hydrogen. This ratio becomes subsequently so changed (being 300 : 100, or even 270 : 100) that the oxygen is scarcely sufficient for the formation of carbonic acid. This lower ratio then remains tolerably constant.

It would appear from the extensive investigations of Regnault and Reiset, that there exists almost one uniform ratio for the most different animals in respect to the composition of the air which is expired during fasting. The consumption of oxygen is invariably less in fasting than in well-fed animals; thus, for instance, 1000 grammes' weight of rabbits, which when fasting absorbed on an average only 0·749 of a gramme of oxygen, took up when well fed as much as 0·877 of a gramme. A much smaller quantity of the absorbed oxygen reappears in the carbonic acid when animals are fasting than when they are abundantly fed upon amylaceous substances. Thus, for instance, in rabbits fed upon carrots, from 84 to 95% of the absorbed oxygen were expended in the formation of carbonic acid, while only from 76·2 to 70·7% were consumed in this manner when the animals were fasting. Regnault and Reiset frequently observed an absorption of nitrogen by animals during fasting; this being almost invariably the case with birds, but of rarer occurrence in mammals.

Bidder and Schmidt* have made two admirable series of experiments on the respiration of cats, when these animals were entirely deprived of solid food. A cat weighing 2464 grammes exhaled 699·52 grammes of carbonic acid (= 190·78 grammes of carbon) and 525·67 grammes of aqueous vapour during 18 days' inanition. A quantitative determination and analysis of the other excretions showed that here, almost exactly as in the case of Regnault and Reiset's direct observations, only 76·5 grammes of every 100 parts of the oxygen absorbed during inanition were eliminated with the expired carbonic acid; and further, that 75·15 parts of aqueous vapour were exhaled with 100 parts of carbonic acid (the animals were very rarely permitted to drink water), whilst 41·72% of the water exhaled were eliminated by perspiration. When we compare the observations made on individual days during this series of experiments, we obtain the following results: the absorption of oxygen decreases constantly to the death of the animal, at first very rapidly (about 2 grammes in the 24 hours during the first few days), and then more slowly and

* Op. cit. pp. 304 et 340.

regularly (about 0·2 of a gramme in the 24 hours till the thirteenth day); this decrease is finally more rapid (about 2 grammes) till the close of the period of inanition. The quantity of inspired oxygen which is not expended in the formation of carbonic acid decreases at first very rapidly, but afterwards with tolerable regularity. At the commencement of the experiment 80% were expended in the formation of carbonic acid (on the second day 77·4%), and at the close of the experiment only 73·0%. The quantity of daily excreted carbonic acid decreases with tolerably uniform rapidity during the first six days, but the diminution is much more gradual during the succeeding six days, and again more rapid during the remaining six days. If, however, we compare the daily excreted carbonic acid with the daily waste of tissue, as calculated by Schmidt, we obtain the following striking relation: at first the quantity of the excreted carbonic acid scarcely amounted to double the quantity of wasted tissue, in the middle of the experiment it was $2\frac{1}{3}$ times as great, and at the close of the experiment it was even triple the amount. This waste of tissue yields, therefore, a relatively much smaller quantity of carbonic acid at the beginning than towards the middle of the period of inanition, but the largest quantity towards the close of the experiment. As we may already calculate from the composition of the fat and from that of the nitrogenous constituents of the body (after deducting the carbon accompanying the nitrogen into the urine and fæces), that the former supplies the respiratory process with 78·1% of carbon, while the albuminates yield only about 46·1%, it will be readily seen that we may easily compute, from the amounts of carbonic acid and nitrogen which are excreted, what are the relative quantities of fat and of albuminates, together with gelatigenous matter, which are daily submitted to metamorphosis. The relation between the quantities of excreted carbonic acid and the loss or waste of tissue, may therefore indicate what proportions of fat and albuminates are consumed during inanition; this is a subject, however, to which we shall presently have occasion to revert.

The quantity of aqueous vapour which is daily exhaled decreases during inanition with tolerable slowness and regularity, but this decrease is somewhat more rapid at the beginning and end of the experiment.

In the second series of experiments (the subject of which was a full-grown male cat, into whose stomach a large quantity of water had been injected), the ratio of the absorbed oxygen to that

which was exhaled with the carbonic acid was almost precisely the same as in the former case, namely 100 : 75·3. There were 95·7 grammes of aqueous vapour exhaled for 100 parts of carbonic acid; only 21·95% of the excreted water was eliminated by the skin and lungs. Whilst, however, in the first case, where no ingestion of water was allowed during inanition, there were daily exhaled on an average 21·641 grammes of carbonic acid for 1000 grammes' weight of the animal, and 16·281 grammes of aqueous vapour; while in the latter case, where water was freely given, 16·30 grammes of carbonic acid and 15·60 grammes of aqueous vapour were yielded by 1000 grammes' weight of the animal; the loss was therefore far less considerable when water was allowed than when both fluid and solid food were simultaneously withheld.

The omission of even a single meal alters the relations of the respiration very considerably, as is clearly shown by Vierordt's observations on the influence of *digestion.* This observer, who was accustomed to dine at half-past twelve, noted the following relations in his own person, which show that the principal meal exerts an influence in this respect which we could scarcely have anticipated.

Time of Day.	Pulsations.	Respirations.	Volume * of 1 expiration.	Air	Carbonic acid	Quantity of carbonic acid in 100 vols. of expired air.
				Expired in one minute.		
Noon	63	10	545·0 c. c.	5450 c. c.	270·22 c. c.	4·69
Two hours after dinner.	78·8	11·22	558·7 „	6162 „	307·36 „	4·74
At 2 P.M., when no dinner had been taken.	62·5	9·5	575·0 „	5479 „	258·18 „	4·73
Difference at 2 P.M., depending upon whether dinner has or has not been taken	16 3	1·72	16·3 „	683 „	49·18 „	0·01

We may see from this table that the individual respiratory functions constantly diminish in activity after the last meal (or in fasting), and that the ingestion of food very rapidly induces a very considerable increase in their intensity; the volume of each inspiration is, however, diminished in the latter case, as we may readily comprehend from anatomico-mechanical relations. Vierordt has, moreover, convinced himself that there is a similar augmentation in the excretion of carbonic acid whenever dinner is partaken

* [The *relative* being of more importance in this table than the *absolute* values, we have not deemed it necessary to reduce the cubic centimetres to inches.—G. E. D.]

of at a different time of the day, and that this increase is both relatively and absolutely greater in the *colder season* of the year. This observation corresponds with the results yielded by the experiments made by Barral* on his own person, in which he found that he excreted one-fifth more carbon through the lungs in winter than in summer.

Scharling also found by his method of experiment that man exhales more carbonic acid under like conditions when he has eaten a full meal than when he is fasting.

It has been proved by various experiments that the products of respiration must also be influenced by *the chemical nature of the food.* This might, indeed, have been conjectured from the experiments of Dulong† and Despretz,‡ on the differences in the respiration of herbivorous and carnivorous animals—results which have recently been confirmed. Dulong found that the ratio existing between the oxygen employed in the formation of carbonic acid and the oxygen which either remained in the blood or combined with the hydrogen, was altogether different in herbivorous and in carnivorous animals, for whilst in the former there was only about 1-10th more oxygen absorbed than was contained in the expired carbonic acid, as much as 1-5th, or even the half of the absorbed oxygen, was employed in the latter for other purposes than that of forming carbonic acid. Lassaigne and Yvart thought they had convinced themselves that guinea-pigs absorb 1-5th more oxygen after nitrogenous than after vegetable food. Letellier found that 1000 grammes' weight of turtle-doves exhaled 136·5 grammes of carbonic acid in 24 hours when fed upon millet, 127·68 grammes after being fed for 3 days on sugar, and only 111·84 grammes of this gas after being fed for 5 days on butter.

The experiments of Regnault and Reiset afford us still further insight into these relations; for these observers found that a much larger quantity of oxygen was employed in the formation of carbonic acid, when dogs had been fed on amylaceous substances than when the food had been of an animal nature; in the latter case only 74·5 of every 100 parts of the absorbed oxygen were found again in the carbonic acid, while in the former case 91·3 parts of the oxygen were employed in the formation of carbonic acid. Nitrogen was also eliminated during a vegetable diet, although in far less quantity than during an animal diet. It is

* Ann. de Chim. et de Phys. 3 Sér. T. 25, p. 165.

† Magendie's Journ. de Physiologie, T. 3.

‡ Ann. de Chim. et de Phys. T. 27, p. 338.

worthy of notice, that a dog which had been fed on mutton suet neither exhaled nor absorbed nitrogen, and that only 69·4$\frac{0}{0}$ of the absorbed oxygen were employed in the formation of carbonic acid. A considerable absorption of nitrogen was observed in hens which had been fed on animal food after several days' starvation, but when they had become habituated to this kind of food they began again to develope nitrogen as in the normal condition: it was also found by experiments on these birds that a far smaller quantity of the absorbed oxygen was found in the carbonic acid when they had been kept on animal food; in two cases there were only 63$\frac{0}{0}$ of the absorbed oxygen present in the carbonic acid which was exhaled. On comparing the different experiments made on dogs and rabbits, we find that, when considered in reference to their dietetic categories, they agree perfectly with the results yielded by Dulong's observations on the respiration of animals. It is also found that after an animal diet the interchange of gases in the lungs is very similar to what we observe during fasting; and this observation, which has also been made in reference to the urine and the other excretions, seems to be explained by the fact that fasting animals to a certain degree live upon their own flesh.

Although our attention is at present most especially turned to direct observations, and although we shall treat fully of the influence of diet upon the molecular movements in the animal body when we enter upon the subject of "Nutrition," the consideration of the question, how far the nature of the food partaken of influences the absorption of oxygen and the excretion of carbonic acid, can scarcely be deemed out of place in the present part of our work. In considering this subject, we have to take our stand upon a postulate, the inductive proof of which we defer for the present; we assume that all the carbon and hydrogen of the fats and carbo-hydrates derived from the food are entirely oxidised in the living body into carbonic acid and water. It must be obvious to all who are acquainted with the composition of these substances, that very different quantities of oxygen are required for their perfect oxidation. The mean composition of the fats is about 78·13C, 11·64H, and 10·13O. The oxidation of the carbon (into carbonic acid) and of the hydrogen, which are contained in 100 grammes of fat, would require (208·35 + 93·92 grammes) = 302·27 grammes of oxygen; but as the fat already contains 10·13 per cent. of oxygen, it would only require to absorb 292·14 grammes of oxygen to effect its entire combustion into carbonic acid and water. When we compare the composition

of sugar with that of fat, we see at the first glance that the carbo-hydrates require far less oxygen for their perfect oxidation than the fats; in the carbo-hydrates there is no hydrogen to oxidise, since the oxygen which they already contain is sufficient for the oxidation of the hydrogen: hence the carbon is the only substance in them requiring oxidation, and this substance is moreover contained in far less quantity in the carbo-hydrates than in the fat for equal weights. Certain organic acids, such as tartaric acid, citric acid, and malic acid, which, as is well known, occur in many articles of food, contain so large an amount of oxygen that it not only suffices for the oxidation of the hydrogen, but in part also for that of the carbon also.

In reference to nitrogenous substances, we cannot, however, grant the postulate that all the carbon and hydrogen is consumed in the animal body, for we know that the greater part of the nitrogen in these substances is not removed in a free state as ammonia, but in combination with carbon, hydrogen, and a little oxygen, by other means than through the lungs. Hence we are led to inquire whether, and to what extent, the nitrogenous nutrient substances yield materials for oxidation, and consequently how much carbonic acid and water they are able to furnish to the respiratory process. As we have already seen that the albuminates and collagen are capable of supporting respiration, we are induced, in explanation of their respiratory value, to adopt the provisional hypothesis that these substances are merely decomposed into carbonic acid, water, and urea in the animal body, although we know that there are formed other nitrogenous products of excretion besides urea. But since the quantity of urea which is produced preponderates very much, and since in many organisms, as, for instance, in the carnivora, urea is almost solely formed, this hypothesis deserves some notice in our consideration of the average value of the amount of oxygen employed in the oxidation of the albuminates and the collagen. We therefore abstract from the composition of the albuminates and other nitrogenous nutrient substances an amount of urea equivalent to the quantity of nitrogen which they contain. If, for instance, we assume that the composition of the albuminates without the sulphur and salts is 54·36% C, 7·27% H, 16·05% N, and 22·32% O, there will remain, after the abstraction of the quantity of urea (= 6·88 C, 2·29 H, and 9·18 O) equivalent to the 16·05 parts of nitrogen from 100 parts of an albuminate, 47·48 parts of carbon, 4·98 of hydrogen,

and 13·14 of oxygen. The following table will give a clearer representation of these relations :—

Substance.	Carbon.	Hydrogen.	Oxygen.	The quantity of oxygen required for the formation of CO_2 and HO, in addition to the amount already present.
100 parts of fat	78·13	11·74	10·13	292·14
„ starch	44·45	6·17	49·38	118·52
„ sugar (C_{12} H_{12} O_{12})....	40·00	6·66	53·34	106·67
„ malic acid (C_4 H_2 O_4)	41·38	3·45	55·17	82·78
„ albuminates	47·48	4·98	13·14	153·31
„ collagen	42·52	4·47	13·59	135·56
„ muscular substance (muscular fibrin + collagen) according to C. Schmidt	46·10	4·72	13·66	147·04

If we consider these relations in their bearing on the development of heat, we shall be able to construct a table such as Liebig long since suggested, which would indicate the different values of these substances in supporting animal heat. Such a calculation may readily be made, if we take as the basis of our computations Dulong's determinations, according to which 1 gramme of carbon develops 7170 units of heat in its combination with oxygen to form carbonic acid, while 1 gramme of hydrogen gives off 34700 units of heat during the formation of water. Although it cannot be denied that in an equation of this kind a number of functions must be taken into account which cannot be deduced from the chemical composition alone, it is, nevertheless, perfectly clear that this is the only point of view from which a rational theory of animal heat can be formed. The present, however, is not the fitting place to enter more fully into this subject. If we limit ourselves to the process of respiration, we obtain, from the above tabular exposition of the different amounts of oxygen required for the complete oxidation of these nutrient substances, certain numbers which may be regarded as *respiratory* equivalents. If, for instance, we assume that an organism in the full performance of its vital functions must absorb 100 grammes of oxygen within a definite time, the following quantities of the above-mentioned substances would be necessary, in union with 100 grammes of oxygen, to satisfy the requirements of vitality: namely, 34·23

grammes of fat, 84·37 grammes of starch, 93·75 grammes of sugar, 120·80 grammes of malic acid, 65·23 grammes of albuminates, 73·77 grammes of collagen, or 68·01 grammes of (dry) muscular substance. No one who has followed our development of physiological chemistry can for a moment suppose that any one individual substance taken from this series can of itself serve the purposes of vitality, provided even it reach the organism in the equivalent quantity; and in the following section our attention will be especially directed to the inquiry of the proportion in which several of these substances require to be mixed in order to render them capable of supporting the vital functions. These numbers must, therefore, remain merely as proportional estimates of their relative values in respect to the functions depending upon the interchange of gases in the lungs.

This table suggests another consideration, which may throw some light upon the difference in the relations between the quantity of oxygen which is absorbed and that which is exhaled in the form of carbonic acid after vegetable and animal food respectively, in as far at least as these relations have been made known to us by the experiments of the inquirers already referred to. If, for instance, we assume that the interchange of gases in the lungs is for a time merely the result of the combustion of a single one of the above-named substances, we should find, whenever pure fat was subjected to oxidation, that for every 100 parts of absorbed oxygen 71·32 parts are contained in the carbonic acid expired during the interchange of gases in the lungs, while in the case of starch and all the other carbo-hydrates 100 parts are found in the exhaled carbonic acid, in malic acid 110·53 parts, and in the muscular substance 83·60 parts. When we compare these numbers with the results obtained by Regnault and Reiset, Bidder and Schmidt, and other investigators, we discover the reason why, after vegetable food, a larger per-centage of the absorbed oxygen is found in the expired carbonic acid than in the case of the carnivora, for the food of the latter class of animals has relatively more hydrogen to be consumed than the food of the herbivora, and on this account we observe that the proportion exhibited in fasting animals, which to a certain extent may be said to live upon their own flesh, is very nearly the same as that noticed after the use of an animal diet.

The above remarks on the influence of the diet generally, show, however, that the *quantity*, as well as the quality *of the food*, exerts a very considerable influence on the amount of the interchange of

gases occurring in the lungs. There must, however, be a certain limit for every organism, beyond which the absorption of oxygen and the excretion of carbonic acid cannot pass. We have already seen (pp. 248-268) that the absorption of nutrient matter from the intestinal canal can only be carried to a certain extent, and we have further convinced ourselves that notwithstanding this limitation of resorption, a far larger quantity of nutrient matters may enter into the mass of the fluids than is necessary for the maintenance of the vital functions; while we finally observe that this excess of absorbed food, when it consist of nitrogenous matters, is very rapidly decomposed in the blood, and that under these conditions large quantities of urea, far exceeding the normal mean, are excreted. But as we have already shown that only a fractional part of the albuminates is eliminated with the urine, while another portion is separated through the lungs, as water and carbonic acid, there can be no doubt that the pulmonary exhalation, as well as the other excretions, is correspondingly augmented after an excessive use of nutrient substances. All the experiments which have hitherto been made in reference to the excretion of carbonic acid in animals that have either been highly fed, or have been artificially fattened, confirmed the above proposition. As we purpose reverting at a future page to this subject, we will only adduce a couple of experiments made by C. Schmidt* on one and the same cat. When this animal was taking 142·41 grammes of flesh in the 24 hours (a quantity which was shown by numerous experiments to be sufficient to maintain the full strength and ordinary weight of the animal), it absorbed 60·14 grammes of oxygen, and exhaled 65·60 grammes of carbonic acid, together with 30·88 grammes of water; whilst during the consumption of 247·32 grammes of flesh it absorbed 103·84 grammes of oxygen, and expired 113·52 grammes of carbonic acid and 47·86 grammes of water. Regnault and Reiset's experiments also exhibit similar results in the case of the herbivora, for we there meet with several cases in which the excess of the absorbed carbo-hydrates may be distinctly recognised by the proportion existing between the absorbed oxygen and that which is excreted with the carbonic acid, this being in many cases as 100 : 95, or even as 100 : 99·7, consequently nearly the ratio (namely as 100 : 100) which accords with the requirements of theory after the use of pure sugar or starch.

The above circumstance leads us to a point, which although it will be considered with all the attention which it deserves under

* Op. cit.

the head of "Nutrition," must not be suffered to pass without some notice in the present place. If, for instance, we consider the ratio of the absorbed oxygen to the oxygen which is again separated (with the carbonic acid), we perceive that it essentially depends upon the quality of the food; but yet after the abundant use of carbo-hydrates the ratio calculated from the above considerations, will never correspond with that which is found by direct experiment: thus, for instance, if we feed an animal on pure starch, we shall never obtain the required ratio of 100 : 100, that is to say, the whole of the oxygen absorbed will never be contained in the expired carbonic acid, because a fraction of it will be expended in the formation of water, for the simple reason that this ratio does not depend solely upon the food, but is modified by the combustion of the nitrogenous organic parts which are destroyed during vital activity. During life those nitrogenous substrata which have been subservient to the functions of the organism, are continually becoming effete and unfitted for further use, and finally reduced to a state of oxidation, for the purpose of being eliminated; these bodies consume a portion of the oxygen in the oxidation of their hydrogen, and, consequently, this portion of the absorbed oxygen is not exhaled as carbonic acid, and the ratio of the absorbed oxygen to the exhaled carbonic acid differs, therefore, from that which we might assume from the composition of the carbo-hydrate. We have thus merely to inquire how much nitrogenous matter is destroyed during the normal course of the vital movements, and what fraction of the absorbed oxygen is consumed by it. To find the amount of this coefficient for every organism, constitutes a problem in the physiology of nutrition. We should, therefore, acquaint ourselves with the typical consumption of the organic constituents in order to find the proportion which essentially expresses the respiratory process, or this respiratory function. If, however, we knew the typical amount of the daily loss of tissue, we might very readily calculate from the quantity of the consumed starch, the relation existing between absorbed and exhaled oxygen. The loss of tissue, consisting of albuminates and collagen yields, as we find from experiments on inanition, the ratio of 100 : 83·6; if now we express the magnitude of the typical consumption of nitrogenous matter by c, and the quantity of the consumed starch by a, the proportional number for the excretion of carbonic acid might very easily be deduced from the formula $\frac{c.\ 83{\cdot}6 + a.\ 100}{c + a}$ The experiments made on fasting animals warrant the conclusion, that the

nitrogenous matters alone in their typical amount c do not suffice for the requirements of the vital functions, but that at the same time a certain amount of non-nitrogenous matter (distinct for each organism) must be subjected to oxidation; when, therefore, the carbo-hydrates are entirely wanting and the albuminates are only sufficient for the restoration of the tissues, the fat is expended in the accomplishment of this object; hence its quantity—the minimum of the necessary non-nitrogenous combustible materials —may easily be calculated, if we know the typical amount of nitrogenous materials undergoing metamorphosis, and the proportion which exists during a state of inanition between the absorbed oxygen and the oxygen which is excreted (in combination with carbon). From the above observations we learn, that the proportional number (for the oxygen in the carbonic acid) after the use of pure fat, is 71·32; if now we designate the typical expenditure of albuminates as c, and the proportional number in a state of inanition be found to be 75·0, we obtain according to the simplified formula $\frac{(83{\cdot}60-75{\cdot}00)\,c}{75{\cdot}00-71{\cdot}32}=x$, the quantity of fat which is consumed together with c albuminates.

We will not extend these remarks, since no further proof is necessary to show how extensively the observations already made on the relation of nutrition to the process of the excretion of carbonic acid may be applied to many other momenta of the process of respiration. We, at all events, obtain some fixed point of support for numerous investigations on the metamorphosis of matter generally.

Although in our considerations of the influence exerted by ordinary food upon the respiration, we have deduced the results of the observations in question from purely chemical relations, we should greatly err were we to adopt the same method in reference to certain substances, which are occasionally introduced with the food into the organism, such, for instance, as the ethereal oils, alcohol, theïne, &c. We do not mean that these substances constitute any exception to this fixed law of nature, but the immediate effect which they produce reminds us that there are nerves in the animal organism which exert the most important influence on all its functions, on nutrition as well as on respiration, and that, consequently, they in some degree disturb that uniform course of phenomena which we might suppose would result from chemical laws. We cannot, therefore, believe that alcohol, theïne, &c., which produce such powerful reactions on the nervous system,

belong to the class of substances which are capable of contributing towards the maintenance of the vital functions. We see this, for instance, in the case of alcohol, which when taken with the food diminishes the pulmonary exhalation instead of augmenting it.

Vierordt, like Prout, found that the excretion of carbonic acid is both absolutely and relatively diminished even after a moderate use of *spirituous drinks*. He has also confirmed Prout's observation, that the increased excretion of carbonic acid which accompanies digestion was considerably checked by the use of spirits. Strong tea exerts, according to Prout, precisely the same result on the respiration as spirituous drinks.

Sleep occasions a very considerable diminution in the excretion of carbonic acid, as we learn chiefly from the experiments of Scharling; thus, for instance, a man who during the day immediately after dinner expired 33·69 grammes, exhaled only 22·77 grammes in one hour during the night; in the case of another man, the ratio of the carbonic acid exhaled during sleep in one hour in the night to that eliminated in one hour in the day after dinner, was 31·39 : 40·74. In experiments on wood-pigeons, I found* that 6·156 grammes of carbonic acid were on an average exhaled during one hour in the morning by 1000 grammes' weight of birds, whilst the same birds expired only 4·950 grammes hourly in the night.

Regnault and Reiset have made observations on the relations of respiration during the hybernation of marmots, which exhibit an enormous difference, compared with the waking state of these animals; thus, for instance, 1000 grammes' weight of marmots absorb in their sleeping state from 0·040 to 0·048 of a gramme of oxygen hourly, whilst in their waking state they consume from 0·774 to 1·198 grammes. In the sleeping animals only 56·7% of the absorbed oxygen pass into the carbonic acid, whilst in the waking state the quantity amounts to about 73%. In two of the three experiments, these observers found that the marmots in their hybernating state exhibited a considerable absorption of nitrogen, whilst they exhaled nitrogen like other animals when in their wakeful state. As a large part of the absorbed oxygen remains in the body of the sleeping animals (since only a small quantity is expended in the formation of carbonic acid, and the water which is formed does not evaporate, owing to the low temperature of the animal), and nitrogen is absorbed, we have an explanation of the

* Jahresber. der ges. Medicin. 1844, S. 39.

fact first observed by Sacc, that the weight of the body is generally, although not constantly, increased during the hybernation of marmots.

These inquirers arrived at similar results in reference to the influence of hybernation, or the sleep induced by exposure to cold, in their experiments on lizards.

It may readily be seen, from the ratio of the oxygen contained in the expired carbonic acid to the inspired oxygen, that only a very small quantity of fat can undergo oxidation in the body of the hybernating marmot (while the nitrogenous substances are still less implicated in the process), for the substance consumed must be far richer in hydrogen; the carbon being to the hydrogen as 21·26 : 5·41, or, according to the atomic weights, very nearly as 2 : 3. (This substance would therefore exhibit a composition not very often met with in organic chemistry, namely, $C_6 H_9 + x H O$.) If, with this abundance of hydrogen, ammonia or any ammoniacal alkaloid should be formed, we need scarcely wonder at the great absorption of nitrogen which Reiset and Regnault observed. At the same time we must beware of drawing too wide a conclusion; for besides the hypothesis already advanced, it would be conceivable, and perhaps more probable, that the oxygen absorbed by these animals during their hybernation combines with only the one part of the hydrogen in one constituent of the body, and thus generates relatively even more water than carbonic acid; thus the atomic aggregate $C_2 H_3$ would be abstracted from such a substance by the inspired oxygen, and the substance itself would not therefore be perfectly oxidised.

Regnault and Reiset found that marmots, when they awake from their hybernation, exhale an extremely large quantity of carbonic acid, and consume more oxygen than at a subsequent period of their waking state—an observation which corresponds with the fact noticed both by Prout and Vierordt in their experiments on man, that the act of waking was followed by a very abundant excretion of carbonic acid, which again diminishes in half-an-hour or an hour.

Bodily exercise increases the exhalation of carbonic acid in the same manner as we have shown that a state of rest diminishes it—a fact which might have been inferred from the above relations of the respiratory movements, but which is also proved by direct observation. Seguin,* one of our earliest observers, found that he

* Op. cit., p. 357.

consumed far more oxygen during violent bodily exercise than during a state of rest. Prout found that at the commencement of moderate exercise there was a relative excess of carbonic acid in the expired air, but during prolonged violent exercise there was less of this gas than in a state of rest. Vierordt convinced himself that the absolute as well as the relative quantity of carbonic acid was increased after moderate exercise, and this result is in perfect conformity with the experiments of Scharling. H. Hoffmann* found that the sum of the products of perspiration of the skin and lungs was much more considerable after prolonged motion than after prolonged rest. Every one who has instituted experiments on the respiration of animals must be aware that they expire far more carbonic acid when they are lively and active than during a state of repose.

Scharling's observations do not entirely exclude the supposition that *mental exertion* may induce an augmented excretion of carbonic acid.

The experiments instituted on man and animals, with the view of ascertaining whether *age* exerts any influence on the respiration, prove that considerable weight should be attached to this relation. Andral and Gavarret, who made tolerably complete observations on the absolute quantity of exhaled carbonic acid, found that the quantity daily expired increases, on an average, to the 40th or 45th year, agreeing mainly with the development of the muscular system. In Scharling's experiments, the two children experimented upon (one a boy aged 9¾ years, and the other a girl of the age of 10 years) expired almost double the amount of carbonic acid exhaled by adults, if we calculate the excretion of carbonic acid for an equal bodily weight; but where the latter is not considered, we find that Scharling's results agree perfectly with those of Andral and Gavarret. The observations made by Regnault and Reiset on animals are also in accordance with these experiments on man, for it was shown that in animals of the same species, for equal weights, more oxygen was consumed by young than by adult animals.

With regard to the influence of *sex* on respiration, it appears, from the experiments of Scharling as well as from those of Andral and Gavarret, that males expire more carbonic acid than females —a relation which obtains even in childhood, for boys eliminate more carbonic acid than girls.

As Scharling's observations must, for the present, to a certain

* Ann. d. Ch. u. Pharm. Bd. 45, S. 242.

extent, be regarded as affording the normal numbers for the excretion of carbonic acid in man, we subjoin his average relations for one hour:—

Subject.	Age.	Weight.	Carbonic acid expired in one hour.	Amount of carbonic acid expired in one hour for each 1,000 grammes' weight.
	Years.	Kilogrammes.	Grammes.	Grammes.
Man	35	65·50	33·530	0·5119
Youth	16	57·75	34·280	0·5887
Soldier	28	82·00	36·623	0·4466
Girl	17	55·75	25·342	0·4546
Boy	$9\frac{3}{4}$	22·00	20·338	0·9245
Girl	10	23·00	19·162	0·8831

According to Andral and Gavarret, an adult man exhales on an average from 38·5 to 40·3 grammes of carbonic acid in an hour; an adult female, when not pregnant, from 22·0 to 23·8 grammes; during pregnancy, 29·3 grammes; and after the cessation of menstruation, from 27·5 to 31·2 grammes. Although Scharling included the products of perspiration with those of respiration, while Andral and Gavarret included only the latter, their numbers are yet higher than those of Scharling. It will be readily seen, from the preliminary remarks which we made on this subject, that the higher numbers obtained by Andral and Gavarret are solely to be referred to the circumstance that in their experiments the respiration was less natural, or at all events more frequent, than in those of Scharling, who, by the use of a commodious apparatus, was enabled to observe a more normal state of the respiration.

Although there can be no doubt that the *bodily constitution* influences the intensity of the respiration, we have no direct observations in proof of this fact, unless indeed we include under that head the fact noticed by Regnault and Reiset, that lean animals consume more oxygen and exhale more carbonic acid than very fat ones—a result which can readily be brought into harmony with the observation made by Schmidt and Bidder, that fat animals excrete far less bile than lean ones.

We now proceed to consider the differences which have been observed in the respiration of different *classes of animals;* for as the greater number of the experiments made on the respiratory functions have been instituted on animals, it is from them that we must derive our most valuable results, more especially from the experiments of Regnault and Reiset, who surpass all other

observers in the value and importance of their results. When we consider, in reference to the *mammalia,* what influence the different food on which they live may have upon the quantitative relations of the interchange of gases in the lungs, we find, on referring to the remarks already made in relation to this subject, that the differences which have been observed in the respiratory relations of the herbivora and carnivora, do not depend upon any difference in their organization, but are almost wholly referrible to the influence of the food upon which they subsist. For in the same manner as we observe that the urine of the carnivora, when fed upon vegetables, is similar to, if not identical with, that of the herbivora, and that the urine of herbivorous animals living on animal substances is analogous to that of the carnivora, we also find that carnivorous animals, which live principally on amylaceous matters, exhibit the same respiratory relations as the herbivora, and conversely. This fact has been proved beyond a doubt by the careful investigations of Regnault and Reiset, and more recently by Bidder and Schmidt. We subjoin a table of these relations as they are given by Regnault and Reiset. We have introduced it here merely by way of furnishing a general retrospect of the whole:—

Species of animal.	Food.	Proportion of 100 parts of absorbed oxygen, which are given off to the carbonic acid.	Consumed Oxygen	Exhaled Carbonic acid	Exhaled Nitrogen
			For 1,000 grammes' weight of the animal in one hour.		
		Per cent.	Grammes.	Grammes.	Grammes.
Dog	Meat	74·5	1·183	1·211	0·0078
Rabbit....	Carrots.	91·9	0·883	1·116	0·0036

The absolute quantity of absorbed oxygen and exhaled carbonic acid is, however, somewhat fluctuating, which partially explains the great discrepancy observable between these results and the numbers obtained by other observers in their experiments on rabbits and dogs. On instituting a comparison between the numbers obtained by different investigators, we find that the results coincide in this respect, that the carnivora, when kept upon their ordinary food, exhale more carbonic acid and nitrogen in proportion to their weight than the herbivora when living upon their ordinary food.

It has long been supposed that the respiration of *birds* was far

more active than that of mammals, but this is by no means an invariable law, and may very probably depend upon the mode of life of the animals; since hens, for instance, which seldom fly, consume very little more oxygen than rabbits, and not even so much as dogs; while the ratio of the absorbed oxygen to the oxygen re-appearing in the carbonic acid is very nearly the same in hens which have been fed upon oats as in rabbits. Very different respiratory relations exist in those more active birds which sing much, are constantly flying about, and seldom at rest except during sleep. Birds of this kind consume more than ten times the amount of oxygen absorbed by proportionally more inactive birds, such as hens, whilst they also exhale nearly ten times more carbonic acid. The experiments of Regnault and Reiset also exhibit a great difference in this respect, that in the more active birds far less oxygen (only three-fourths) is employed in the formation of carbonic acid; but this ratio may, however, probably be dependent upon the fact that in the experiments in question the birds were fasting, being alarmed and off their feed. Regnault and Reiset, moreover, refer the great absorption of oxygen and exhalation of carbonic acid to the smallness of these animals, and connect it with the greater necessity for heat in the smaller animals. Although* I was long since led by my own experiments to express the view, that the excretion of carbonic acid in birds stood in an inverse ratio to their size, it appears to me that the necessity for heat may afford the most available ground on which to explain this fact. The cause must undoubtedly be sought in the greater activity and in the consequently more rapid metamorphosis in the more active birds, although it is unfortunately only the smaller varieties which can be employed for such experiments. If we were able to investigate the respiratory equivalents of vultures and other large birds of prey, which continue for a long time on the wing, and if we could examine them under their natural relations, we should most certainly find them much greater than in the case of hens, ducks, geese, &c. Nature may, however, have endowed smaller birds with greater energy and a more rapid metamorphosis, in order to enable them to maintain the same temperature of body as larger birds.

The smaller birds whose respiratory equivalents we have given in the following table from the mean results of Regnault and Reiset, were green-finches, crossbills, and sparrows.

* Jahresber. der ges. Med. 1843 u. 1844, S. 39.

Animals.	Food.	Of 100 parts of absorbed oxygen, there pass into the carbonic acid	Consumed Oxygen	Exhaled Carbonic acid	Exhaled Nitrogen
			For 1,000 grammes' weight of the animal in one hour.		
		Per cent.	Grammes.	Grammes.	Grammes.
Hens.	Oats. Abundantly	80·7	1·053	1·320	0·0079
Small birds	Sparingly	75·3	11·473	11·879	0·1296

The *eggs* of birds also maintain a process of respiration, even in the unincubated state ; fresh eggs, on exposure to the air, continuously exhale carbonic acid and aqueous vapour, and hence they lose considerably in weight when kept for some length of time. But they also absorb oxygen, as is more especially shown by the circumstance that the air inclosed in the air-space contains more oxygen than atmospheric air, according to Bischoff* from 0·22 to 0·245$\frac{0}{0}$, and according to Dulk† from 0·25 to 0·27$\frac{0}{0}$ (by volume); but this has been denied by Baudrimont and Martin St. Ange. The process of respiration becomes more active after incubation, as is obvious from the circumstance that the development of the embryo is very soon arrested and that death ensues in hydrogen or carbonic acid gas, as is shown by the experiments of Viborg, Schwann,‡ and Martin St. Ange. The greater part of the oxygen in the air-space disappears during incubation, and the air is then frequently found to contain about 6$\frac{0}{0}$ of carbonic acid. The more recent experiments of Baudrimont and Martin St. Ange§ have shown, in reference to the interchange of gases during the incubation of hens' eggs, that in proportion as the embryo becomes more fully developed, a larger amount of oxygen is absorbed from the atmosphere and more carbonic acid given back to it. Here also the quantity of oxygen contained in the carbonic acid falls far short of the absorbed oxygen. The experiments of Valenciennes have proved that here too the respiration is accompanied by a liberation of heat. The following table gives the results of the experiments, instituted by two of the observers already referred to, on eggs; but here the total loss of weight in the eggs, owing to the chloride of calcium in the apparatus, no doubt greatly exceeds the normal quantity.

* Schweigger's Journ. N. R. Bd. 9, S. 446.

† Ibid. 1830, p. 363.

‡ De necessitate aëris atmosph. ad evolut. pulli in ovo. Berolini, 1834.

§ Compt. rend. T. 17, p. 1343.

In 1,000 grammes' weight of eggs.	From the 9th to the 12th day of incubation.	From the 16th to the 19th day of incubation.
The loss of weight amounted to	26·26 grammes.	41·72 grammes.
The absorbed oxygen	5·74 „	10·70 „
The exhaled carbonic acid	4·33 „	11·92 „
The exhaled water	2·88 „	3·66 „
The ratio of absorbed O to the O in CO_2	100 : 54·9	100 : 81·0

Spallanzani also found that even the egg-shells alone absorbed a little oxygen and exhaled carbonic acid—a circumstance, however, which presents a much closer analogy with the decomposition of other substances, such as fibrin, &c., than with the respiration.

In considering the respiration of the *amphibia*, we shall merely refer to the experiments of Regnault and Reiset (notwithstanding the admirable observations of Marchand, which we have frequently noticed), as their results could alone furnish us with numbers admitting of comparison with the above tables, in as far as they have been obtained by one and the same method. In all main points, however, these observers perfectly agree with one another.

Animals.	The per-centage of oxygen entering into the carbonic acid.	Oxygen. consumed	Carbonic acid exhaled	Nitrogen exhaled
		By 1,000 grammes' weight of the animal in one hour.		
	Per cent.	Grammes.	Grammes.	Grammes.
Frogs	76·0	0·084	0·0880	0·0005
Salamanders.	82·4	0 085	0·0960	——
Lizards	75·2	0·1916	0·1976	0·0025

We find, even amongst the amphibia, that the more active creatures exhibit greater rapidity in the metamorphosis of matter, and therefore consume more oxygen and exhale more carbonic acid and nitrogen, than the more sluggish animals, in which there is a less active metamorphosis of matter. This relation is very strikingly shown, in the above table, between lizards and frogs. This requirement of the amount of the respiration is further confirmed by certain experiments made on lizards; in the first experiment the animals were perfectly rigid, in the second they were not entirely rigid, and in the third, the results of which are given in

the table, they were fully awake and lively. The half torpid animals consume about three times, and the perfectly wakeful animals nine times the amount of oxygen required by those which were in a perfectly rigid state. The same relation exists in respect to the absolute quantity of the excreted nitrogen, although we very frequently meet with the opposite condition in these animals, namely, with absorption of nitrogen, as was several times noticed in frogs by Regnault and Reiset.

We now proceed to investigate the products of respiration of those animals which do not respire through lungs, namely, insects and fishes. Although the former of these absorb atmospheric air directly, the mechanism of inspiration and expiration is not the same as in lung-breathing animals. Their pneumatic apparatus consists of extremely elastic ramifying tubes, intersected by vessels of communication designed for the uniform distribution of the air. The expiration in insects is effected by muscular action only, while the act of inspiration is accomplished solely through the elasticity of the tracheal walls, which not only consist of chitin, but are surrounded by a spiral thread of that substance for the purpose of increasing their elasticity. The air in the tracheæ is brought into free and direct contact with the external atmosphere by means of the so-called stigmata, in which there is not often any appearance of muscularity. By every motion of the insect the universally distributed tracheæ are compressed, and a portion of the air which they contain is thus expelled; when the muscular contraction ceases, the tracheæ, in consequence of their extreme elasticity, resume their former volume, and fresh air again enters through the open stigmata into the spaces containing rarefied air. Insects are also provided with a special muscular apparatus for expiration, but this is limited to the abdominal rings, and exhibits even in beetles only 15 or 25 contractions in a minute, corresponding pretty nearly with those of the dorsal vessel. The voluntary and irregular motions undoubtedly exert the most important influence on the expiration of the air in insects, and hence we find that the various degrees of animation in the motions of insects produce the most extraordinary differences in respect to the quantity of carbonic acid which they excrete, and the degree of animal heat which they exhibit. On this account pupæ expire only 1-190th or 1-160th part of the carbonic acid which is exhaled by a caterpillar of equal weight; but yet, according to Regnault and Reiset, the consumption of oxygen by the larva of the silkworm is only about 1-20th less than that by the caterpillar.

Regnault and Reiset, as well as myself, have experimented on the respiration of insects, as had been previously done by Spallanzani, Saissy, and Treviranus.

Reiset and Regnault employed cockchafers and the caterpillars of the silkworm when near the time of spinning, for their experiments on the respiration of insects. Their results were as follows:—

Animals.	The per-centage of oxygen entering into the carbonic acid.	Resorbed oxygen	Exhaled carbonic acid
		For 1,000 grammes' weight of the animals in one hour,	
Cockchafers	80·8	1·0195	1·1372
Silkworms	78·2	0·8990	0·9600

In my own experiments on the excretion of carbonic acid in insects, I obtained* the following results for 1000 grammes' weight of the animals for one hour:—

	Mean.	Minimum.	Maximum.
Cockchafers (5 experiments)	0·729	0·650	0·832
Caterpillars of Phal. Bomb. Neustria (8 experiments)	0·896	0·603	1·138
Caterpillars of Phal. Bomb. Dispar (7 experiments)	1·077	0·835	1·303
Caterpillars of Pap. Nymph. Urticæ (2 experiments)	0·0070	0·0069	0·0071

The respiration of animals breathing through *gills*, as fishes, crustaceans, &c., differs from that of creatures breathing through lungs or tracheæ, inasmuch as already dissolved oxygen is conveyed to the blood or the nutrient fluid, from which the dissolved carbonic acid must be removed. The mechanism by which the oxygenated water is propelled to the gills, and that which is loaded with carbonic acid is again removed, is so complicated, that mere indications of its character would carry us beyond our limits. There have unfortunately been but few experiments instituted with

* Op. cit., p. 42.

gill-breathing animals since Humboldt and Provençal prosecuted their experiments on the respiration of fishes. We find from these observations, which were most admirable for the time at which they were undertaken, that also in this form of respiration the oxygen which is absorbed exceeds that which is exhaled in the form of carbonic acid, the latter amounting in these experiments to scarcely four-fifths of the absorbed oxygen, and frequently to only half the quantity. These experiments yield, however, this remarkable result, that fishes constantly absorb very large quantities of nitrogen: and they show that fishes, like other animals, transpire copiously through the skin. These animals, moreover, are capable of breathing in atmospheric air as long as their gills are moist, the products of respiration presenting under these circumstances the same relations to the absorbed oxygen as in water, which is an obvious proof that respiration in water-breathing animals follows the same laws as those which control atmospheric respiration. Baumert* has recently, by the aid of an ingenious apparatus, made several interesting experiments on the respiration of the tench (*cyprinus tinca*), the gold-fish (*cyprinus aureus*), and the pond-loach (*cobitis fossilis*). It was shown by these experiments, in the first place, that 1000 grammes' weight of tench inspired on an average 0·0143 of a gramme of oxygen in one hour, and exhaled 0·0138 of a gramme of carbonic acid; while, on the other hand, the same weight of the more lively gold-fish absorbed 0·0409 of a gramme of oxygen, and eliminated 0·0419 of a gramme of carbonic acid in the same period of time. The ratio of the volume of absorbed oxygen to that of exhaled carbonic acid was very nearly as 10 : 7; for every 100 grammes of absorbed oxygen 72·3 grammes are again expired with the carbonic acid. In reference to the nitrogen, Baumert found sometimes a slight absorption, and sometimes a slight exhalation. In experiments with the pond-loach, results were obtained differing in several respects from those which we have been describing; thus, for instance, this fish, like some others, exhibits a special intestinal respiration, for it absorbs air through the mouth as well as by the gills, swallowing it on the surface of the water, and thus conveying it to the stomach. Baumert analysed the air which was again eliminated through the intestinal canal, and found that it contained much less oxygen than the air which the fish had swallowed; the oxygen had, however, been replaced by much less carbonic acid

* Chem. Untersuch. über d. Respiration des Schlammpeizgers. Heidelberg, 1852.

than we usually meet with in bronchial or pulmonary respiration. The oxygen which is absorbed by the intestine passes, therefore, into the mass of the blood, and the carbonic acid to which it gives rise is not eliminated by the intestine, but through the gills; hence we also find, from Baumert's experiments, that in the bronchial respiration of these animals there is a far greater exhalation of carbonic acid in proportion to the inspired oxygen, than in the previously-named fishes. Special observations further showed that the pond-loach very seldom employs the intestinal respiration in fresh water, which contains a richer supply of oxygen, although in water which is poor in this gas, it very frequently comes to the surface in order to swallow air; yet these animals do not appear capable of supporting life by only one of these functions; they sicken when respiring through the gills only, almost as quickly as when they are limited to intestinal respiration. The experiments which were made upon pond-loaches by the same method employed with the tench and gold-fish yielded the following results: 1000 grammes of pond-loaches inspired on an average 0·0316 of a gramme of oxygen, and exhaled 0·0543 of a gramme of carbonic acid in the hour; these animals, therefore, gave off more oxygen in the form of carbonic acid than they had absorbed through the gills; since for 100 parts of oxygen absorbed through the gills, 124·9 grammes were eliminated with the carbonic acid. This result fully agrees with the comparative analyses made by Baumert of the air which was swallowed, and that which was again excreted through the intestine; for whilst the air in the intestine showed a diminution of the oxygen amounting to 8 or 11% by volume, the carbonic acid had only increased about 2% at most. Baumert's analyses have further shown the probability that pond-loaches always absorb a certain quantity of nitrogen during respiration.

Of those animals which possess no special organs of respiration, but accomplish their necessary interchange of gases by the skin only, the earthworm is the only one which has been made the subject of experimental investigation, and the only experiments of the kind, which we possess, were made by Regnault and Reiset. They prove that the respiration of these animals is very similar to that of frogs, which also respire vigorously through the skin. The consumption of oxygen, and the ratio of the oxygen contained in the carbonic acid, are nearly the same as in the latter animals: 1000 grammes' weight of worms absorbed in one hour 0·1013 of a gramme of oxygen, and exhaled 0·0982 of a gramme of carbonic

acid; the ratio of the absorbed oxygen to that in the carbonic acid is as 100 : 77·5.

As in all these experiments on animals, the *cutaneous perspiration* has been investigated at the same time with the *pulmonary exhalation*, it might be supposed that no very exact result could be obtained for the latter, but the above numerical values are correct enough for the higher animals, as mammals and birds; for the inexactness is here so slight, that it generally falls short of the fluctuations in the errors of observation and other irremediable or incalculable conditions. In the case of rabbits, dogs, and hens, Regnault and Reiset have, indeed, adopted two methods for the more accurate determination of that portion of the gaseous excretion of the animal body which escapes through the skin; in both cases the animals were inserted in an air-tight bag, and their mouths alone were allowed to come in contact with the atmosphere; in one case the air within the bag was changed; in the other it was left undisturbed. In the first mode of experiment hens yielded only from 0·0047 to 0·18 of the carbonic acid resulting from the whole perspiration, rabbits only from 0·0102 to 0·0173, and dogs from 0·0035 to 0·0041. The second method also showed that the influence of cutaneous perspiration and intestinal exhalation is very unimportant when compared with the pulmonary function in the warm-blooded animals.

The relation between cutaneous transpiration and pulmonary exhalation must not, however, be considered so unimportant as it might appear from these experiments on thick haired and densely feathered animals. The gaseous exhalations from the skin in man have scarcely been examined, but the quantitative investigations hitherto made, as for instance, those of Valentin, prove that the human skin takes a very considerable part in the separation of aqueous vapour from the body. This fact had already been rendered very probable by certain dietetic and other observations, and seemed to derive confirmation from Magendie's method of making the skin of animals wholly impermeable by means of glue, paste, varnish, &c.; and although the death of the animals thus experimented upon cannot be referred solely to the retention of gaseous fluids, the latter, although inconsiderable in quantity, are not devoid of importance in a physiological point of view. There are indeed many questions which still demand our earnest attention in reference to this subject; and even if the life of an animal of higher organization could continue to exist in a relatively normal state for any length of time after cutaneous exhalation had been

suppressed, this circumstance would prove as little the unimportance of cutaneous gaseous transpiration, as the interesting experiments of Regnault and Reiset, on frogs whose lungs had been extirpated, could prove that the lungs of frogs are superfluous organs. In these experiments the frogs not only continued to exist for a very long time, but they also consumed a considerable quantity of oxygen (although scarcely as much as half the amount consumed by the uninjured animals): thus, for instance, 1000 grammes' weight of these animals consumed in one hour 0·047 of a gramme. The ratio of the oxygen to the transpired carbonic acid and to the nitrogen was nearly the same as in the uninjured animals.

This leads us to the consideration of the abnormal phenomena which the interchange of gases in the lungs occasionally presents, and which are consequent on anomalies, functional or other derangements of individual organs, or diseases. This subject is, however, beset with so many difficulties that we have hitherto been obliged to content ourselves with the determination of the absolute or relative quantity of excreted carbonic acid, and even these limited experiments have not yet led us to any important results.

In entering upon these *pathological* relations we cannot pass over an accurate observation made by Bidder and Schmidt,* although we shall recur to it more fully in the following paragraph; we allude to an experiment on the respiration of dogs, in which all the bile was carried off externally by means of a biliary fistula. For every kilogramme of this dog, which was kept almost entirely without food, there were absorbed in one hour 1·146 grammes of oxygen, and 1·146 grammes of carbonic acid were exhaled; hence, of every 100 parts of absorbed oxygen 77·07 were returned with the carbonic acid: for every kilogramme of a dog operated upon in this manner, but receiving an abundant supply of flesh, there were absorbed in one hour 1·153 grammes of oxygen, while 1·327 grammes of carbonic acid were excreted; hence, of every 100 parts of absorbed oxygen 83·7 parts were contained in the carbonic acid. We simply give these numbers in the present place as facts, since we purpose analysing this experiment more fully in a future page.

Three different methods have hitherto been proposed for the investigation of the interchange of gases in the lungs during morbid conditions; but these are unfortunately nearly all equally open to objection. In the first place, animals were experimented upon, in which certain abnormal processes had been induced by the opera-

* Op. cit. pp. 368-386.

tion employed, as was done by Regnault and Reiset, and in part also by Bidder and Schmidt. In these experiments, as in most cases in which animals were experimented upon, the whole amount of the perspiration was determined by inclosing the animals in a receiver to which fresh air was conveyed, while the air already used was carried off by a system of vessels for the purpose of being absorbed. I have myself* made experiments of this kind on the process of inflammation. The most important obstacle to such inquiries in the case of animals, is that many diseases which are of the greatest importance in the eyes of the physician, cannot be produced by operations, or any other artificial means. There are very few places, moreover, in which the experimentalist has the opportunity of carrying on a series of investigations on spontaneously diseased animals. On this account, the human subject has hitherto been most frequently experimented upon, for the sake of investigating the process of respiration and its effects on the excretion of carbonic acid in disease. Hannover† has partially co-operated with Scharling in employing the last-named method for determining simultaneously the pulmonary and the cutaneous perspiration. This method is undoubtedly the best adapted for examining the respiration during disease, provided the patients can, without any inhuman aggravation of their condition, bear to be moved and temporarily confined within a closed receiver. It cannot be denied that even in this mode of experiment, the true effect of disease upon the exhalation of gas is unavoidably modified, at least during an experiment of short duration, by the mental excitement of the patient; but this evil is far less completely rectified in Prout's method, which has been followed by Malcolm,‡ Hervier and St. Sager,§ and Doyère.|| It demands considerable practice to acquire the facility exhibited by Vierordt, in breathing with perfect calmness into an apparatus, however well it may be constructed; the disease may often run its course before the patient is able to acquire the necessary proficiency, while on the other hand humanity forbids us to torture a fever-patient for any length of time with such experiments. Hence great caution should be exercised in deducing scientific conclusions from any observations of this kind. Then, moreover, in the experiments made according to the

* Abhandl. d. Begründ. d. k. sächs. Ges. der Wiss. 1846, S. 465.

† De quantitate acidi carbonici ab homine sano et ægroto exhalati. Havniæ, 1845.

‡ Monthly Journ. of Med. Science. January, 1843.

§ Compt. rend. T. 28, p. 260; Gaz. des Hospitaux. 1849, p. 85.

|| Compt. rend. T. 28, p. 636.

last-named method, the determination has almost always been limited to the relative amount of carbonic acid in the air, without regard to the volume of the expirations, and hence we need hardly observe that such experiments are scarcely of any value.

My experiments on the *process of inflammation* and its influence on the perspiration have been unavoidably limited to rabbits, in whom it is very difficult to excite an acute inflammation. I found it was not sufficient merely to wound the animals, and that it was necessary at the same time to inject stimulating substances into the wounds; but notwithstanding these measures, I always had to make several fruitless attempts before any individual animal could be brought into the condition necessary for these experiments. I subjoin only the results of those experiments to which I attach the greatest importance, and in which the morbid phenomena, as well as the composition of the blood, indicated the presence of the process of inflammation.

In (*a*) and (*b*) the lungs were the seat of inflammation, and in (*c*) and (*d*) the inflammatory process extended over several muscles.

(*a*) In every three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :—

Before the animal was wounded, and during three hours in the morning	3·820	grammes.
Immediately after being wounded	3·877	„
On the first day	2·951	„
„ second day	3·217	„
„ third day	2·308	„
„ fourth day	1·838	„
„ in the evening	1·731	„

(*b*) In every three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :—

Two days before being wounded	3·170	grammes.
Immediately after being wounded	3·392	„
On the first day	3·199	„
„ second day	2·914	„
„ third day	1·877	„

(*c*) In three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :—

Two days before being wounded	3·592	grammes.
Immediately after being wounded	3·947	„
On the first day	3·533	„
„ second day	2·711	„
„ third day	2·179	
„ fourth day	2·098	„

(*d*) In three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid:—

Immediately before being wounded	3·004	grammes.
Twelve hours after	2·941	„
On the second day	2·986	„
„ third day	2·213	„
„ fourth day	2·347	„
„ fifth day	2·066	„

According to P. Hervier and St. Sager, many acute inflammations, such as meningitis, peritonitis, metritis, and acute arthritic rheumatism, yield an excess of carbonic acid (*hypercrinie carbonique*), and all inflammations in which the respiration is implicated, as pneumonia, pleurisy, and pericarditis, yield less than the normal quantity of this acid (*hypocrinie carbonique*).

But what opinion can we form of experiments which, like those made by Hervier and Sager, have led to results diametrically opposed to the best observations, and which have exhibited distinctions of such extreme delicacy, that other observers have been unable to arrive at such nicety of observation, even when employing more exact methods? What are we to think when we see that these experimentalists found that less carbonic acid was exhaled during the period of digestion than in a state of fasting; that they distinguished two maxima and two minima of the exhalation of carbonic acid, of which the one maximum occurred at 9 o'clock in the morning, the other at 11 o'clock at night, while the one minimum was observed at 3 o'clock in the afternoon, and the other as early as 5 o'clock; that they observed the quantity of excreted carbonic acid constantly rise with the pressure of air, and found invariably more carbonic acid exhaled after animal food than after a vegetable diet, and even without in any way investigating the proximate coincident causes?

According to these experimentalists, moreover, the excretion of carbonic acid is augmented in the cold stage of intermittent fever, and still more so in the hot stages. "When the patients perspire, the air they exhale hardly varies from the ordinary air. Again, the normal relations of the excretion of carbonic acid remain unchanged in all chronic diseases combined with fever, as in chlorosis, diabetes, the beginning of cancer, nervous affections, and chronic inflammations. The quantity of consumed carbon falls in measles, scarlatina, roseola, erythema, during the period of suppuration, in scurvy, in purpura, anæmia, anasarca, the last stages of cancerous, scrofulous, or syphilitic degenerations, in typhus, dysen-

tery, chronic diarrhœa, and pulmonary phthisis. The temperature of the expired air rises and falls with the number of the respirations." This confused assemblage of names of diseases and symptoms, and of obsolete and recent titles of disease, sufficiently attests the nature of these investigations.

Hannover has attempted to determine the quantity of carbonic acid exhaled in chlorosis; he employed four girls in these experiments, which so far admitted of comparison with Scharling's observations, that three of these girls were of nearly the same age as the girl experimented upon by the latter observer; the fourth girl, when in a state of perfect health, and at the age of 17 years, expired 0·4546 of a gramme of carbonic acid in one hour for every 1000 grammes of her weight. Hannover's three chlorotic patients, whose respective ages were 15, 16, and 18 years, exhaled, according to similar calculation, 0·6666, 0·6105, and 0·5874 of a gramme, and, consequently, an amount of carbonic acid far exceeding the quantity eliminated by the healthy girl. This fact is the more worthy of notice as there is reason to believe that the blood-corpuscles participate in the absorption of oxygen, and in the formation of carbonic acid, although in those cases in which it has been proved with tolerable certainty that the blood-corpuscles are considerably diminished, it has been found that the excretion of carbonic acid is increased rather than diminished. Although we are not quite justified in concluding from this fact, that the blood-cells are devoid of all influence on the formation and excretion of carbonic acid, it is quite certain that they do not contribute very essentially to the interchange of gases, and that the source of the carbonic acid, as we learn from other experiments, has to be mainly sought in the metamorphoses of the tissues, and only to a very slight degree in the processes occurring in the blood-cells. Moreover, in these chlorotic patients, the absolute quantity of the excreted carbonic acid stood in an inverse ratio to the number of the respirations, which, as we have already seen, is the reverse of what we observe in the normal state. Hannover was unable to discover any increase of animal heat, notwithstanding the great development of carbonic acid; indeed, chlorotic patients generally complain much more of cold than of heat.

All these experiments of Hannover were conducted with the greatest care in every respect; for besides making a very accurate examination of the special form of disease, he very carefully noted in each respiratory experiment the numbers of the pulsations and respirations, the temperature, the height of the barometer, the

bodily weight, and the age and constitution of the individual. All the experiments were made in the middle of the day between 10 and 1 o'clock, and the patient was in no case suffered to remain more than half an hour in the apparatus. The observations were made principally between the months of September and December.

Hannover instituted experiments on the respiration of five persons suffering from pulmonary tuberculosis; the tubercles being in part already softened and suppurating. The absolute amount of carbonic acid generally increases with the number of the respirations, while the relative amount (that which is contained in a definite volume of air) diminishes. The other experiments made by Hannover on the excretion of carbonic acid in some other morbid conditions, are too disconnected to admit of our deriving any definite results from them.

Doyère repeatedly examined the air expired by a young girl who had cholera, and continued his observations till the death of the patient; he found that the excretion of carbonic acid was generally much diminished in this disease, and that this excretion was augmented as soon as the general condition of the patient improved.

Malcolm instituted a more exact series of experiments, according to Prout's method, on this relation in typhus, in which he, of course, determined only the relative quantity of carbonic acid in the expired air. This observer found that in nineteen cases of mild typhus the quantity of carbonic acid contained in 100 volumes of the expired air, varied between 1·18 and 4·15; the mean of all these observations gave the number 2·492%, but this quantity fell to 2·232% in seven more severe cases of typhus. Prout gives 3·96% as the mean number for persons in health; the relative amount of carbonic acid in the expirations is therefore very considerably diminished in typhus. The amount of carbonic acid in the air cannot be brought into any definite proportion either to the number of the respirations or of the pulsations.

Here again we perceive the great deficiencies of pathological chemistry, which does not even supply us with the necessary materials for establishing a system. On the other hand, it must be admitted that the charge of inapplicability to medical practice, which has been advanced against this section of physiological chemistry, is less just in the case of the respiration than in the theory of digestion (see p. 308). Until recently, the determination of the respirations, and of the contractions of the heart in cases of disease, were little more than mere symbols, which nothing but

the rudest empiricism could venture to adopt as explanations for the recognition, diagnosis, and prognosis of diseases, whilst at the present time, although our knowledge of the interchange of gases, and the influence of the movements of the respiration and the circulation may not always afford definite conclusions, it can, at least, supply us with certain indications of the most essential constituents of the pathological process, by which we may regulate and modify our medical treatment. The more exact knowledge of the respiratory functions which we now possess has thrown a clearer light on the process of fever than any of the innumerable treatises which have been written on the subject. We are indebted to pure physiological investigations for numerous elucidations of some of those groups of symptoms which we meet with in certain diseases, such as pulmonary tuberculosis, emphysema, certain heart-diseases, diabetes, &c. No one can deny that the great advance which has been made in modern times in respect to our knowledge of respiration, has afforded us a deeper insight into these and many other pathological processes, but it would carry us too far were we to enter more fully into the results yielded in this respect by pure physiology to pathology. It is in his practice by the bedside that the physician obtains the most important aid from the physiology of the respiration. We do not exaggerate when we assert that there is scarcely a page of this section on the respiration which does not treat of facts from which the physician may obtain the most valuable hints for his treatment of various diseases, and more especially of pulmonary affections.

While the advances of the science of medicine have taught us that of all the vast accumulation of remedies which in the course of time have been collected together, very few are of any value at the bedside, and while the enlightened practitioner is disposed to attach at least as much importance to a rational dietetic as to a specifically therapeutic mode of treatment, the value of investigations on normal respiration, in reference to the science of medicine, can never be over-rated; for when once the fact is universally admitted that the first thing to be considered in many diseases is to furnish a copious supply of oxygen to the blood which has been loaded with imperfectly decomposed substances, and to remove as speedily as possible the carbonic acid which has accumulated in it, these observations will have afforded us true remedial agents, which exceed almost every other in the certainty of their action. We may perhaps aid a tuberculous patient quite as much by recommending him to respire a moist warm air, as if

we prescribed *Lichen Carragheen*, or *Ol. jecoris Aselli*. Instead of tormenting an emphysematous patient, suffering from congestion and hæmorrhoidal tendencies, with aperients and saline mineral waters, we might relieve him far more effectually by recommending him to practice artificial augmentation or expansion of the chest in respiration (filling the lungs several times in the course of an hour), or to take exercise suited to produce this result, while we should forbid the use of spirituous drinks, and not prescribe tinctures, which might hinder the necessary excretion of carbonic acid. We abstain, however, from offering any further illustrations of these assertions, since the reflecting physician will not blindly follow any guide; while the mere empiricist can never learn thoroughly to heal any disease, whatever may be his knowledge of physiology and pathological chemistry.

We endeavoured, at the beginning of this section, to give a general representation of the interchange of gases which occurs within the lungs, tracing the movements of the atmospheric air into the pulmonary vesicles, where an opposite current of gases is developed from the fluid blood. What we then regarded almost *à priori* as a physical necessity in this occurrence of two opposite currents of air, has been proved, from Vierordt's experiments, to be an actual fact. Mechanical forces, considered in the strictest sense of the word, were insufficient to carry the oxygen into the pulmonary vesicles and the carbonic acid into the trachea, as has been most conclusively proved by the suggestive experiments of Hutchinson* and others. There is one portion of their course through which the oxygen and carbonic acid must be propelled by the aid of diffusion; and this, as Vierordt has shown by the numerous modifications of his experiments on respiration, is controlled by the same laws which Graham† has expounded in so masterly a manner. We may, therefore, hope that we have arrived at the recognition and physical explanation of the interchange of gases effected within the air-passages. We have thus, as it were, arrived at the boundaries of the blood in our theoretical consideration, and it now only remains for us to explain the physical or chemical laws by which the gases dissolved in the blood are liberated, and those of the atmosphere are condensed in the blood. Having acquainted ourselves with the constitution of the air at the place of its exchange—that is to say, in the pul-

* Medico-chirurgical Transactions, Vol. 29, pp. 137-152; and Cyclopædia of Anatomy and Physiology, Vol. 4, pp. 1016-1087.

† Trans. of Roy. Soc. of Edin. Vol. 12, p. 222.

monary vesicles—we have next to ascertain the character of the blood which is affected by this interchange of gases; for without a knowledge of its character, before and after this interchange, we shall be unable to form an opinion of the principles which control this most essential part of the process of respiration, that is to say, the interchange of gases between the blood and the air in the pulmonary vesicles.

Two questions present themselves to our notice in entering upon such considerations, regarding the manner in which, on the confines of the air and the blood, as it were, this interchange is effected between the carbonic acid and the oxygen: one of these questions is, *whence does the blood derive its carbonic acid*, and in what form does it convey this gas to the lungs? The second question is, in what physical or chemical relations does the oxygen stand to the blood, or to this or that constituent, in its passage into the blood? In considering the first question as to the sources of carbonic acid in the animal organism, we must, in the first place, remember that all animal fluids contain gases, and especially carbonic acid. We have already seen, in the second volume of the present work, that carbonic acid, oxygen, and nitrogen, are present not only in the blood, but also in the lymph, the transudations, the parenchymatous juices of many organs, and even in the urine. It is by means of these juices that all the animal tissues, as well as the parenchyma of the organs, are permeated by the gases in question, and there is not a single vital organ in the whole animal body from which we might not, by means of the air-pump, extract free carbonic acid, nitrogen, and some traces of oxygen. An experiment which was begun long ago in my laboratory placed this relation, as might readily have been conjectured *à priori*, beyond all doubt, by affording a positive proof of the quality of this gas; we are, however, still deficient in the more exact quantitative determinations for individual organs.

But when we investigate the source of the carbonic acid in the blood, and incline to the belief, after the most general examination of the vegetative vital functions, that it must, in part at least, be sought in the activity of the different organs themselves, we cannot wholly refute the objection which might be offered, that the carbonic acid may be formed in the blood itself, and be conveyed with the transudations of this fluid into the parenchyma of the organs. It is, therefore, in the first place necessary to prove *the pre-existence of this carbonic acid in the fluids of the tissue.* The probability of such a pre-existence may readily be seen by

analogy, and the fact has been almost directly proved by positive observations. We have purposely devoted more time to the mechanism of the respiration of insects than we generally give to the mechanical relations of the animal processes; for it is precisely in these animals which have no true blood, but merely parenchymatous juices, and no true blood-vessels, but at most mere rudimentary hearts, or a very limited analogue, the so-called dorsal vessel, that the atmospheric air penetrates directly through the most delicate tracheal ramifications to the very elements of the organs; here the air does not come first in contact with the blood, nor does it pass for any length of time with it through vessels, where it may undergo metamorphoses accompanied by a development of carbonic acid gas; the carbonic acid must here be formed in the parenchyma of the organs themselves, and through their vital activity; for the amount rises and falls in the exhaled air, as we learn from direct experiments, almost in equal proportion to the amount of the activity of these organs. It is, therefore, probable that also in the higher animals endowed with true blood, the carbonic acid is almost entirely formed in the functional organs, and not in the liquor sanguinis. And should we then find such great differences in relation to the amount of the gases, in the character of the blood flowing to and from the organs (the arterial and venous blood), if all the carbonic acid of the blood flowing to the right side of the heart were formed gradually and alone throughout the whole extent of the blood-column passing from the left to the right side of the heart through the capillaries? No further probabilities need be adduced to prove that the parenchyma of the organs is the seat of the formation of carbonic acid, as we obtain the most convincing proof of the correctness of this view from the admirable investigations of G. Liebig.* Although many points may be susceptible of improvement in the method of experimenting adopted by G. Liebig, the main results must continue unaffected. We have already (p. 95) noticed the most essential facts which have been brought to light by these inquiries. We would here only repeat, that the carefully prepared frogs' muscles absorb oxygen and exhale carbonic acid so long as their irritability or contractility lasts, that the latter is lost in irrespirable gases, and finally, that a muscle completely deprived of blood continues to maintain this interchange of gases so long as it retains its contractility. We have here, therefore, not the mere representation, but the perfect expression of a respiration of the organ of a

* Ber. d. Akad. d. Wiss. zu Berlin, 1850, S. 339-347.

higher animal without blood, and even without any special air-passages; the interchange of gases and the formation of the carbonic acid originate here directly from the organ from which the carbonic acid is otherwise conveyed to the atmosphere by various indirect means (and necessarily through the blood and lungs). As, moreover, these experiments show that the muscles cannot retain their activity without an access of free oxygen, at all events, a large portion of this gas must, after its absorption by the lungs, be conveyed in a free state through the blood and the walls of the capillaries into the muscles. The blood is, therefore, quite as well adapted to convey to the muscles the free oxygen necessary for the accomplishment of their functions as to carry off the carbonic acid formed by this function; the *first interchange of gases* is, therefore, effected in *the parenchyma of the organs* themselves or if we regard the interchange of gases between two different media as the process of respiration, the first act of this process—the first interchange—is effected between the parenchymatous juice and the blood in the capillaries. This act may be compared to the respiration of water-breathing animals; the difference consisting almost solely in this, that the medium conveying the oxygen is on an average denser than the medium which is destined to absorb oxygen, or that the difference in the density of both is on the whole very small, whilst in the true water-breathing animals the density of the receiving medium exceeds that of the water very considerably, but principally in the circumstance that the blood differs essentially from water in its great capacity for the absorption of oxygen and carbonic acid. Notwithstanding this difference, we may hope that when the respiration of animals breathing through gills has been sufficiently elucidated (and this subject is at present occupying the attention of Valenciennes), we may succeed in bringing this interchange of gases, which is effected through the walls of the capillaries of the greater circulation, into accordance with the laws of the transfusion of the gases absorbed by fluids. Then only can we establish the theory of this portion of the respiration on physical grounds.

Before we proceed to consider the second act of respiration in the higher animals, that is to say, the interchange of gases in the capillaries of the lesser circulation and the pulmonary vesicles—the interchange between the blood and the air—we must not omit to inquire *whether all the oxygen in the arterial blood is free*, and whether all the carbonic acid in the venous blood is only mechanically combined. The previous experiments, as well as the obser-

vations of Magnus and Marchand, to which we have already referred, and according to which the fresh blood exhibited no chemical attraction from oxygen, might incline us to believe that all the oxygen absorbed by the blood in the lungs passed unchanged, that is to say, uncombined, into the capillaries of the greater circulation, and from thence into the parenchyma of the organs. This, however, is by no means the case, and we have already given the reasons, which seem to show that a part of the absorbed oxygen enters into chemical combinations even in the arterial blood. We need here only refer to the peculiar relation of the crystalline substance of the blood towards gases [see note to vol. i, p. 373 in the Appendix], and to Liebig's apodictic proof, that as the blood considered as a fluid can mechanically absorb only a very small portion of oxygen, the greatest part of the oxygen which disappears during respiration must of necessity be chemically absorbed.

The very careful and admirable experiments of G. Liebig* appear at first sight to oppose the idea of a chemical absorption of the oxygen in the lungs; for he found that the differences of temperature in the different parts of the circulating system, including both the arterial and the venous systems, were solely referrible to the physical laws of the radiation of heat, &c., and that in the lungs especially, the blood not only undergoes no elevation, but even a slight depression of temperature.

Here, therefore, we obtain for the first time, through G. Liebig's investigations, a direct confirmation of the early hypothesis, that the blood is cooled in the lungs by respiration. This fact appears, as has already been stated, to stand in direct opposition to the assumption that the oxygen is chemically absorbed, at all events in part, in the arterial system. This discrepancy is, however, merely apparent, as we may readily perceive, when we consider that only a part of the oxygen that enters the blood is chemically absorbed, that a great part of the free heat is consumed in the restoration of the carbonic acid to its gaseous form and in the evaporation of water, that the specific heat of water is very great, and that the difference of temperature between the blood in the left side of the heart and that of the right side is extremely small. If we follow G. Liebig's experiments in their details, more especially in reference to the testing of the methods of observation, and observe how the temperature of the blood in the different

* Ueber d. Temperaturunterschiede d. venösen u. arteriellen Bluts. Inaug. Abh. d. Med. Fac. zu Giessen vorgel. 1853.

vessels is dependent upon external physical effects, we might rather wonder at the slight diminution of the temperature in arterial blood, and apply this observation in support of the assumption of a chemical absorption of oxygen.

Although we can scarcely any longer entertain the slightest doubt that a large portion of the absorbed oxygen enters into chemical combinations in the arterial blood, we are not on that account justified in assuming that *carbonic acid* and water are already *formed* within *the arterial blood*, for this is an assumption which has already led to many erroneous theories regarding the respiration. As the serum is only capable of absorbing a small quantity of oxygen, and as we find that the blood-corpuscles change so essentially in the capillaries, the more probable view will always be, that the oxygen is conveyed from the blood-corpuscles to the capillaries in a loosely combined state, and that it passes from thence into the parenchymatous fluids in order there to commence effecting oxidations, among the products of which we find carbonic acid and water. We have already endeavoured to show that wherever oxygen and organic matters enter into combination, they do not at once yield carbonic acid and water as the products of their combustion, and that these simple oxides (as in putrefaction and decomposition) are often only simply separated from the oxidised body, without the organic body being entirely destroyed, as in combustion. We must, however, beware of adopting such an exclusive view as to maintain that there is no generation of carbonic acid or even of water within the lungs, or between the left side of the heart and the capillaries, after the oxygen has been absorbed in the blood. We might more readily adduce proofs of the formation of a part of the carbonic acid after the first contact of the blood with the atmosphere, than the contrary. Magnus has certainly found relatively less, but absolutely more, carbonic acid in venous than in arterial blood; and although we may not regard this individual observation as one of constant occurrence, we can scarcely interpret it in any other way than that, at least in this case, carbonic acid is developed after the access of oxygen to the venous blood. In fact, we must obstinately adhere to a pre-conceived opinion, if, notwithstanding the important differences recently made known to us in the arterial and venous blood, we should still maintain that the blood remains wholly unaffected by the oxygen with which it is charged in the lungs, and that any one of its constituents cannot intimately appropriate to itself the oxygen without losing it again in the

capillaries. When we fully consider the differences exhibited in the blood before and after the absorption of the oxygen in the lungs (see vol. ii., pp. 248 and 259), we shall find some difficulty in yielding to the opinion, that the parenchyma of vitally active organs is the only destination of the oxygen.

We will simply remark in conclusion, that the very decisive influence of the different nutrient substances on the process of respiration, which we have shown to exist, cannot be reconciled with the view, that all oxidation must take place in the parenchyma of the organs. The carbo-hydrates, as well as the excess of albuminates, are very quickly oxidised, as might be conjectured, from the pulmonary and urinary excretion; these substances, which are absorbed in what may be termed superfluous consumption, are not first converted into constituents of the organs to be again excreted; but whether they are first conveyed from the blood and carried into the innermost parts of the organs in order to be consumed, is a question which we are not yet able to decide; there seems at the present day to be every appearance of probability that the greater part of the carbo-hydrates and fats, and the excess of albuminates, are decomposed and oxidised within the course of the blood.

Now that we have convinced ourselves, in the course of our inquiries, that that interchange of oxygen and carbonic acid, which we term respiration, is a process which is not limited to any individual part of the animal body; and now that we have seen how, on the one hand, an interchange of air is effected in the air-passages by the double means of mechanical transport and by diffusion, and how, on the other hand, an active interchange of gases takes place in the parenchyma of all the organs and in their capillaries, it simply remains for us to ascertain *the laws* which control *the interchange* between the elastic *gases* of the air conveyed to the lungs and the condensed gases of the blood of the pulmonary capillaries *upon the humid mucous membrane of the pulmonary vesicles.*

We shall wholly pass over the older *theories* regarding the process of respiration, as they were almost exclusively mere hypotheses based on few facts, and consequently not explanations considered in a scientific point of view; nor, indeed, were such explanations possible at that time, when scarcely a conjecture had been hazarded in reference to the laws of absorption, of diffusion, and many other physical principles bearing upon this subject. Although we can scarcely yet venture to hope that we are

acquainted with all the physical laws which may come into play in the interchange of gases in the lungs, our exposition of the positive facts referring to the respiration sufficiently show that we have nearly succeeded in tracing to their physical fundamental requirements the individual sections into which the respiratory process may be divided. The first attempt to determine the physical law according to which the blood and the air interchange their gases in the lungs was made by Valentin in conjunction with Brunner, and conducted with equal intelligence and perseverance. Valentin arrived at the result, that this interchange of gases corresponds perfectly with the *law of the diffusion of gases* established by Graham, and that consequently the oxygen and carbonic acid are interchanged in an inverse ratio to the square roots of their densities. As it does not fall within the limits of the present work to enter into more diffuse theoretical expositions, we will here content ourselves with briefly indicating the difficulties which oppose the unconditional assumption of this theory. In the interchange between the gases of the blood and the air in the lungs, we meet with external relations differing wholly from the conditions under which Graham observed the interchange of gases through a porous partition wall, and on which he based his law; after what has already been stated, it would appear almost superfluous to observe, that in respiration an absorbed gas is opposed to an elastic fluid gas, while in the process of diffusion both gases must be in the elastic fluid state and under equal pressures, which cannot be the case in the respiration. These and some other points, which are opposed to the direct application of the law of diffusion to the respiration, might perhaps be of less importance if this interchange of carbonic acid and oxygen occurred in the ratio required by the law of diffusion, that is to say, that 85·16 vols. of carbonic acid should be interchanged for every 100 vols. of oxygen. If this ratio very frequently exists during an animal diet, we have nevertheless encountered numerous facts in our previous observations which appear to be diametrically opposed to this law; a law cannot, however, tolerate an exception, and when the latter can be shown to exist, the law is without force. It seems to us at least that many of the facts which have been proved beyond a doubt by the most recent investigations, notwithstanding all the concessions which might be made in favour of the peculiar animal relations, cannot be brought entirely into harmony with Valentin's theory.

Vierordt has described the interchange of gases on the inner

surface of the lungs in a manner corresponding entirely to known physical laws as well as to positive facts; there are few theories in physiology which have resulted from such numerous and carefully conducted experiments as those which Vierordt established, and which he based upon the laws of absorption discovered by Henry and Dalton. Henry has shown that the quantity or the volume of an absorbed gas depends entirely upon the pressure under which the gas above the fluid remains after the absorption has been completed; while Dalton has proved that in the mixed gases the pressure of each individual gas, which, as is well known, is entirely independent of that of the intermixed gases, alone determines the proportion in which this gas is absorbed by a fluid. If, therefore, there be more carbonic acid contained in the blood than the pressure of the carbonic acid in the pulmonary vesicles is able to maintain in a state of condensation, a corresponding quantity will escape from the blood, until the amount of carbonic acid in the blood is reduced to the number corresponding to the amount which would be absorbed by blood containing no carbonic acid, and exposed to a tension equal to the carbonic-acid pressure on the pulmonary vesicles. The quantity of carbonic acid thus passing into the pulmonary vesicles would therefore depend, in part, upon the quantity of this gas condensed in the blood, and in part upon the tension of the carbonic acid gas already contained in the air of the pulmonary vesicles. Under the relations occurring in the animal body a motion in a directly opposite direction would be imparted to the oxygen. The blood, when it enters the lungs, is not sufficiently saturated with oxygen, and is able, under the pressure which it then experiences, to absorb a larger quantity of this gas; the tension of the oxygen contained in the pulmonary vesicles is so considerable, that a portion of it is transferred into the blood, and there condensed. Both gases are therefore quite independent of each other, as the more correct physical explanation would lead us to infer; their interchange is not effected by mutual displacement, but is determined for each gas by the quantity of condensed gas in the blood, and by the tension of the corresponding elastic fluid gas contained in the air of the pulmonary vesicles.

There can be no doubt whatever that this law of Dalton applies perfectly and completely to the free gas contained in the blood (whether mechanically combined or absorbed), and hence it must constitute one of the most important factors in the interchange of gases in the lungs; but we have already seen that a very

large portion of the so-called free oxygen and carbonic acid gas in the blood is in a state of unstable chemical combination, and hence Dalton's law can, strictly speaking, only apply to the fraction of carbonic acid and oxygen contained in the blood which is only mechanically absorbed, or, to express the same thing in different words, is merely taken up by the water in the blood. The law of absorption is not, however, of less importance to the theory of respiration; and we may perhaps be justified in assuming that all the oxygen is mechanically absorbed (in accordance with the above-mentioned law) before it enters into this unstable chemical combination, and that the carbonic acid, before it is separated from the blood, is mechanically dissolved from its chemical combination, when the diminished external pressure favours, or rather controls, its elimination. It cannot, however, as yet be strictly proved that the membranes which separate the blood and the air within the lungs may not manifest different degrees of permeability towards the gases or the fluids which saturate them, and may not, therefore, exert some influence on the interchange of gases proceeding in accordance with the law of absorption; for although these membranes may be extremely thin, they yet consist of at least three delicate layers of tissue, namely, the pavement epithelium and the membrane propria of the pulmonary vesicles, and the walls of the capillaries. The great difference of permeability shown by animal membranes towards fluids, having even the same character, makes it not unreasonable to conclude that, if we could once succeed in establishing a general formula for the expression of the interchange of gases in the lungs, this function would constitute a part of it.

The effects of the respiration on the entire metamorphosis of animal matter, and on the individual functions of the latter will be systematically considered in the following section. It is customary to associate the theory of *animal heat* with that of the respiration, for, since the time of Priestley and Lavoisier, flame has not been regarded merely as a poetical symbol of life, but life and combustion have been regarded as two perfectly similar processes. Lavoisier's theory of animal heat has experienced various modifications in the course of time and from the pressure of advancing science, as has also the theory of combustion, although both are true in their fundamental principles. We will not here enter more fully into the theory of animal heat, since it still rests on a very uncertain foundation, and since further an accumulation of the various facts and arguments bearing upon the subject would

extend our work to an unreasonable size. Besides this, it is still questionable whether the theory of animal heat, which embraces so many purely physical and purely physiological laws and facts, can, strictly speaking, be considered as pertaining to physiological chemistry; for, if we admit its claim to this rank, we might with equal justice be called upon to enter into a more detailed exposition of the theory of animal electricity, since this, no less than the theory of animal heat, is based upon chemical inquiry. We ought to observe, however, that the special heat of every animal organism is merely the result of chemical combinations formed within it. No one has elaborated this proposition with more argumentative ingenuity and ability than Liebig; and nothing but excessive incredulity, combined with an inadequate knowledge of physical laws, could lead any one to doubt the correctness of his exposition. Dulong* and Despretz† are, however, almost the only inquirers who have afforded us any positive investigations in relation to the main point of this subject; and according to their observations, only from seven to nine-tenths of the heat generated in the organism can be referred to oxidation. Too much importance must not, however, be attached to these results, for it must be admitted that the method of investigation employed by these inquirers was not entirely free from blame, while, moreover, they exhibited extraordinary instability in their estimate of the number of the units of heat developed from the carbon, as well as from the hydrogen, during oxidation. If, however, future investigations should enable us to become better acquainted with the heat that is evolved from the combustion of the carbon and hydrogen (and especially to determine it with accuracy in those cases where, as in the animal organism, the elementary atoms to be burned must be only gradually dissolved by the oxygen from very complicated compounds), and if repeated zoo-calorimetric investigations, free from the errors of the above-named physicists, should lead to the desired result, that the animal heat which is developed entirely corresponds to the quantity of carbon and hydrogen burned in the body, then it would indeed appear most wonderful that other chemical excitants of heat, which are sufficiently obvious to every one, should be altogether excluded from the animal organism. Why should the chemical union of acid and base, and the many decompositions and other processes,

* Ann. de Chim. et de Phys. 3 Sér. T. 26, p. 1-86.

† Ibid. 2 Sér. T. 26, p. 54-110.

which, as we know, are generally accompanied with the development of heat, lose this property in the animal body? This much is established and placed beyond all doubt by the labours of the most trustworthy observers, that the chemical movements in the living body are more than sufficient to explain the animal heat, and particularly that the process of oxidation which is carried on through the respiration yields by far the most important contribution to its excitation. Attempts have been made to ascribe to the nervous system a share in the production of heat, but, as we have already observed in vol. i., p. 17, we cannot form a conception of the nervous system in a state of action without chemical changes occurring in it. Any one may observe the depression of temperature that ensues in parts in which the connexion between the nerves and the central nervous system has been interrupted; and we are well acquainted with the recent experiments of certain French physiologists, who, after dividing the sympathetic at a certain spot, have found the animal heat, at definite parts, considerably higher than the ordinary temperature,—an observation which I have myself had occasion to make; and while we do not overlook the difficulties which oppose an explanation of such phenomena in a special case, we must regard every view as unscientific, and therefore incorrect, which would refer the origin of animal heat, although only partially, to any other than chemico-physical forces.

If, however, the chemical theory of heat, as it has been generally understood, is open to objection, it seems to us that it can only arise from its having been regarded less as the consequence than as the object of all, or, at any rate, of most of the chemical movements in the organism. Animal heat has, perhaps, been brought too prominently forward in the consideration of the metamorphosis of animal matter, so that it may almost have appeared as if a great number of the animal processes were accomplished solely for the purpose of generating heat in the living body. When we inquire into the objects accomplished in the organism, animal heat acquires a special significance from the fact, that most of the higher animals, however they may otherwise differ, are endowed with a power of compensation, which is so carefully adapted to each, that even the most different external or internal relations are scarcely able to produce the slightest fluctuations of temperature. The conclusion which we might be led to draw from this fact, in reference to the importance of animal heat for the vital functions, is certainly some-

what shaken by the consideration, that many of the so-called cold-blooded animals from the agility of their movements, the nature of their food, their respiratory equivalents, the energy of their growth and nutrition, in short, from the amount of their metamorphosis of matter, are not so far different from mammals and birds as to establish the necessity of this high degree of temperature for the maintenance of life, and the energetic performance of the most essential vital functions. And are we not arguing in a circle, when we assert that animal heat is subservient to the metamorphosis of matter, and that the latter again is subservient to the promotion of animal heat? If we were to assume, that this high degree of temperature is necessary for the formation of the tissues from nitrogenous food, as well as for the functions of the organs, and that amylaceous substances are taken up in the organism merely for the purpose of generating this degree of temperature, the cold-blooded animals, which are not inferior to higher animals in rapidity of growth, and not unfrequently equal them in the energy of their vital functions, would, even under such limitations, refute these conclusions. If the carbo-hydrates were consumed by animals merely for the purpose of generating heat, it seems teleologically incomprehensible why certain fishes, whose animal heat never rises above the surrounding medium, even after the most active movements, should live almost exclusively upon amylaceous matters. (We need only instance the case of gold-fishes, which live for years on no other food than wafers.) We have already endeavoured (pp. 216–221) to indicate the objects which may be fulfilled by the carbo-hydrates beyond that of generating heat in the animal body. We do not, however, intend by these remarks to disparage the importance of animal heat in relation to life. All the admirable investigations which have led us to recognise an internal connection between respiration, certain nutrient matters, and animal heat, have afforded us a deeper insight into the vital processes; and hence it is no poetical imagery to connect the life of respiring beings in reference to their production of heat with the process of combustion. Animal heat does not, however, on that account occupy a higher place than every other phenomenon, and every other result which is manifested in the active living organism; at once an effect and a cause, it proceeds, as in combustion, from processes on which it exerts a favourable reflex action; it is only one, but not the highest link of that immeasurable series of phenomena which constitute the true substance of corporeal existence, and is

in certain organisms nothing more than the inevitable consequence of the chemical processes of the animal organism—nothing more than the final result of a movement regulated by definite laws.

We have purposely referred in brief terms to the different theories of the respiration, as a fuller exposition of theoretical questions and discussions would have been foreign to the plan of this work (as we have already observed in our methodological introduction); hence it has mainly been our object to limit ourselves to the notice of facts which have become incorporated with science, giving a critical opinion of their value wherever it was practicable to do so.

We have, therefore, endeavoured as far as possible, to consider the scientific bases on which physiological chemistry has been raised to the level which it *now* occupies. We purpose in the succeeding and closing section of this work, to notice the facts which have led to the deductions of this or that theoretical conclusion, without entering into a full exposition of the numerous theoretical questions which are discussed at the present day. Nor do we think that the time has yet arrived when a complete system of the metamorphosis of animal matter can be given in a text-book of physiological chemistry, and we should even be exceeding the widest limits allowed to such a work, were we to take part in the contest which is still waging concerning many of the leading questions of the metamorphosis of animal matter, for as we have already frequently remarked, the noblest labours of many distinguished physicists show that we are still deficient in the first exact physical and chemical bases of a theory of the metamorphosis of animal matter. We abstain the more readily from a further discussion of this subject, as we should otherwise be compelled to add to the three volumes, of which our work already consists, still another, which notwithstanding the exact bases laid down in the three former volumes, must of necessity be a mere repetition of the individual views of the author. All, therefore, who desire to acquaint themselves with the discussions on the more general views of vegetative life must familiarize themselves with the ground of the contest, and learn for themselves, by carefully testing the evidence on both sides, how to reach a higher and more comprehensive point of view. But those who do not feel that they possess the power of entering into such discussions, either as judges or combatants, will adopt the safest course if they accept the interpreta-

tions of one, who by his great discoveries in this department of science, as well as by his extraordinary powers of combination, has earned the right to be heard; we need scarcely say that we refer to Liebig. For even when facts were wanting, and when the empirical data were unsettled and vacillating, the acuteness of his intellect has frequently revealed secrets in nature which have rarely failed, on subsequent investigation, to verify the correctness of his views.

Nutrition.

We have already, in the beginning of this work, advanced the proposition, that the study of the process of nutrition was the crowning point or final aim of all our researches in physiological chemistry; but although all our previous considerations and all our researches tended ultimately towards this point, we are still far removed from it, nor shall we find that our exertions have been rewarded with the success we might have hoped to achieve. Even here we are compelled to rest satisfied with a mere sketch, which notwithstanding a few sharply defined outlines, is still so imperfect that it must be left very much to the imagination of individual inquirers to fill up the deficiencies according to their own conception of what is needed for its completion, not forgetting that the colours which are thus superadded must soon merge, according to circumstances, into other tints, and can only be fully realised by those who are familiar with the subject.

In the course of our considerations we have acquainted ourselves with all the substrata in which the animal processes are effected; we next endeavoured to ascertain the mutual relations of the different substrata and processes in the accomplishment of the most essential functions of animal life, both in their general and special conditions, and we sought to study the parts assigned by nature to each of the four great groups of substrata, or to their individual members, within the animal organism. It would scarcely, therefore, appear necessary to enter into any elaborate exposition or investigation of those matters, which are necessary to the continuation or maintenance of vital motion when once induced, for that which has once been exhausted can necessarily be replaced

only by something similar or identical. This restitution must be regulated according to the expenditure. Although these propositions are almost too self-evident to be advanced, yet it required the most extensive, laborious, and exact investigations of the most intelligent inquirers to arrive at the result which now seems to us to be so simple and so easy of attainment, namely, that the requirements of the animal organism in the accomplishment of the vital functions, must correspond with those four groups of substances which, as we have already delineated in the above sketch of the motions of animal matter, constitute their essential and fundamental elements. But this need scarcely excite our wonder, since it has required all the researches and investigations embraced within the entire compass of this work to effect this object. Is any one link of this long chain of so slight an importance that it does not stand in the closest relation to the general process of vitality? It is only by means of all these introductory propositions that we are able to comprehend how those substances, which we have learnt to know as the most important adjuncts in the metamorphosis of animal matter, must also be contained in those matters which the animal body takes up for the renovation and restoration of that which has been lost or rendered effete (whether it be a fluid or a tissue, a ponderable or an imponderable matter), and for the regular accomplishment of the vital phenomena.

There could scarcely be a doubt that the albuminous matters, the fats, the carbo-hydrates and salts, which we have learnt to know as the bases of the metamorphosis of animal matter, must at the same time serve as the nutrient matters of the animal body; yet the opinion that one of these groups was more important than another to the vital process has led to many errors in reference to the physiological value of the nutrient matters. It was long before it could be conclusively shown by experiment, that the value of any of those bodies could only be expressed by the combination of these four categories. How far we were removed, even a short time since, from comprehending this simple truth, is sufficiently proved by the various experiments prosecuted under the direction of different learned societies, in which animals were fed exclusively on nitrogenous matters, as for instance, albumen or animal jelly; and the result of these observations excited general surprise, when it was found that in those experiments, which had been conducted with the greatest exactness, the animals perished under symptoms of inanition, and exactly as if they had been deprived of all food.

The nutrient quality of any one substance depends upon the intervention of some other body ; and it is only by the reciprocal action of these four fundamental substances that life can be maintained, even as it was originally begun and influenced by the same means. We ought, therefore, to distinguish, in our consideration of the absorption of matter necessary for the maintenance of life, between those essential *nutrient matters* which we have learnt to know as adjuncts in the metamorphosis of matter and those *articles of food,* which originating either in the vegetable or animal kingdom, generally contain the former in combinations of the most varied proportions. This is, however, so obvious, that after what has been already advanced, it would be superfluous to enter further into the subject. But if the various articles of food differ to so extraordinary a degree in the amount of nutrient matters belonging to these four groups, it would not seem out of place to estimate the value of food by the proportion in which these substances are combined in them, so as best to promote nutrition. However justly the albuminous matters may be termed histogenetic or organo-plastic, and however indispensable they may be to the vital organs, we must necessarily ascribe a very limited nutritive force to all articles of food which in addition to the albuminates contain neither fats nor carbo-hydrates, and even if all these matters were combined together in one article of food, we could scarcely ascribe to it any great degree of nutrient force, unless there were also phosphates and other salts present in it, for no cell or fibre could be formed or regenerated without the co-operation of these salts. If, therefore, all four groups of nutrient substances are equally necessary to afford compensation to the animal organism for the matters which have become effete, or to supply materials for the establishment of new manifestations of force, those articles of food will be the best and the most invigorating which consist of such substances combined in the proportion which is best adapted to the animal organism. Hence we see, that the idea of *the nutritive value of any article of food* is entirely relative, as it depends partly upon the proportion in which the four fundamental bases of nutrition are mixed in it, and partly upon the individual requirements of the organism that is to be nourished.

There are, therefore, two points which specially demand our attention in entering upon a scientific consideration of food generally, and of its nutritive qualities specially; the first refers to the amount of these four elements, which it contains; and the second, to the circumstances under which the organism exhibits a

greater or lesser necessity for one or more of these elements, for the maintenance of its integrity, as well as for the production of certain effects of force. These questions must be solved by quantitative determinations, for the physiologico-chemical statistics of the living organism are not alone competent to elucidate this subject. We need scarcely observe, that in judging of the nutritive value of an article of food, we must not lose sight of the quality of the nutritive elements belonging to the different groups, since this in a great measure determines its digestibility. Hard-boiled white of egg, meat that has been boiled for a long time, and hard cheese which is poor in fat and in salts, are less easily digested than soft-boiled or fresh white of egg, meat steeped in vinegar, or slightly coagulated moist and rich cheese; starch is much more rapidly converted into sugar when boiled than in its raw form, when, as we have already seen, it frequently and principally passes off in an unchanged state, whilst another carbo-hydrate, namely cellulose, is only employed as food by certain animals under special relations. Notwithstanding their identity of constitution, the members of the same group frequently exhibit very great differences, depending upon their greater or lesser accessibility to the agents of digestion. An article of food may, therefore, owing to the indigestibility of its constituents, frequently possess a far less nutritive value than we should expect from the mixture and composition of its elements of nutrition. It must not, therefore, be wholly forgotten, that the digestibility of a substance constitutes one of the factors of its nutritive value. As, however, this subject closely corresponds with all that has already been stated in reference to the digestibility of the different nutrient matters, we will now revert to the main questions already noticed, the former of which considered the proper admixture of the individual elements of nutrition in the nutrient substance. Before we proceed to decide the question of what are the most favourable proportions of these four fundamental nutrient matters in any one article of food, (and, therefore, how the normal nutrient matter must be constituted in order, under the common relations, to yield to the animal organism the materials necessary for the fulfilment of all its functions, as well as for the renovation of effete matters,) it will not be out of place to consider from this point of view the composition of the ordinary articles of food.

As the nitrogenous constituents of the nutrient matters, that is to say, the albuminates, are principally employed in the reproduction of the tissues, and of the actual organs of the animal organism,

investigators, amongst whom Boussingault ranks foremost,* have more especially directed their attention to the amount of these matters contained in the food. As vegetable food commonly contains only very small quantities of other nitrogenous matters besides the albuminates, it was thought that the nitrogen they contained would afford a proximate measure of the value of these matters in reference to the reproduction of the tissues, and, therefore, to one of the most important parts of the metamorphosis of matter. Besides Boussingault, Thomson,† and more especially Schlossberger ‡ and Horsford,§ in part under the direction of Liebig, have made tolerably extended investigations in relation to this subject. Liebig has, moreover, suggested the institution of very complete investigations in reference to the other classes of nutrient matters, with a view of determining the quantity of the carbo-hydrates or starch and of salts contained in a number of different articles of food; Horsford and Krocker || have made the most admirable observations in respect to this point. As the numbers obtained in these inquiries are of the highest importance to nutrition in more than one point of view, although it is not possible to give a comprehensive list of them, we are induced contrary to our usual custom, to give the fundamental values found by these different observers. 100 parts of the thoroughly dried substances yielded the following results :—

Boussingault found	Nitrogen
In rice	1·39
„ potatoes	1·5
„ turnips	1·7
„ carrots	2·4
„ rye	1·7
„ maize	2·0
„ barley	2·0
„ wheat	2·2
„ oats	2·2
„ peas	3·8
„ lentils	4·4
„ beans	5·1
„ haricots	4·5

Thomson found	Nitrogen
In white bread	2·27
„ brown bread	2·63
„ Glasgow unfermented bread	2.17
„ Essex flour	2·17
„ Canada flour	2·21

Schlossberger and Döpping found	
In Agaricus deliciosus	4·6
„ „ russula....	4·2
„ „ cantharellus	3·2

* Economie rurale. Paris, 1844, p. 483.

† Phil. Mag. 1843. Vol. 23, p. 323.

‡ Ann. d. Ch. u. Pharm., Bd. 52, S. 106-120, and Arch. f. physiol. Heilk. Bd. 5, S. 17-28.

§ Ann. d. Ch. u. Pharm. Bd. 58, S. 166-212.

|| Ibid. p. 212-227.

Schlossberger and Kemp found :—

	Nitrogen.
In cows' milk	3·78
„ woman's milk	1·59
„ Dunlop cheese	6·03
„ Dutch Gouda do.	7·11
„ Cheshire do.	6·75
„ double Gloucester do.	6·98
„ old Gloucester do.	5·27
„ yolk of egg	13·44
„ oyster	5·25
„ liver and bile of crab	7·52
„ raw Mussel (Mytilus edulis)	8·41
„ boiled do.	10·51
„ liver of the ox	10·66
„ pigeon's liver	11·80
„ portable soup	12·16
„ raw eel	6·91
„ boiled do.	6·82
„ eel extracted with boiling alcohol	14·45
„ raw salmon (Salmo fario)....	12·35
„ boiled do.	9·70
„ salmon extracted with alcohol	15·62
„ raw herring	14·48
„ boiled do.	12·85
„ herring extracted with alcohol	14·54
In the milt of herring	14·69
„ raw haddock (Æglefinus communis)	14·64
„ boiled do.	12·98
„ haddock extracted with alcohol	15·72
„ raw flounder	14·18
„ boiled do.	15·18
„ flounder extracted with alcohol	15·71
„ raw skate (Raja batis)	13·66
„ skate extracted with alcohol	15·22
„ crab	13·66
„ raw pigeon	12·10
„ boiled do.	12·33
„ pigeon extracted with alcohol	13·15
„ raw lamb	13·26
„ lamb extracted with alcohol	14·56
„ raw mutton	11·30
„ boiled do.	13·55
„ mutton extracted with alcohol	14·76
„ raw beef	13·87
„ beef extracted with alcohol	14·88
„ raw ham	8·57
„ boiled do.	12·48
„ ham extracted with alcohol	14·21
„ the white of hens' eggs	13·44

Among the interesting conclusions which may be drawn from these investigations, we will simply refer to the observation which had earlier been made by Schlossberger, *that the amount of nitrogen in muscular fibre does not essentially differ throughout the whole animal kingdom.* The *flesh of fish* contains the same absolute amount of nutrient matter as that of the higher animals; *oysters* on the contrary, in opposition to the general view, contain far less, and hence the difference between the absolute amount of nutrient matter and the amount of easily digestible matter is most clearly shown.

We need, however, scarcely observe, that we cannot judge directly from the amount of nitrogen contained in animal nutrient matters regarding their direct value in the reproduction of the blood and tissues. For the nitrogen, which is found, depends in part upon the gelatigenous matters of the animal nutrient substances; it is, however, still very doubtful whether the gelatinous substances can contribute anything towards the reproduction of the tissues, although it may at least be seen with certainty from

their composition that they cannot fulfil the same objects as the true albuminous substances.

The following table gives the results of those investigations of Horsford which were at the same time directed to the elucidation of the amount of ash and sulphur contained in vegetable food :—

FOOD.	Percentage of Nitrogen.	Percentage of Sulphur.	Percentage of Ash.	Percentage of calculated Albuminous Substance.	Percentage of calculated Non-nitrogenous Substance.	Percentage of Water in the fresh food.
Wheat-flour from Vienna, No. 1	3·00	0·23	0·70	19·16	79·77	13·85
" " No. 2	2·12	0·15	0·66	13·54	85·37	13·65
" " No. 3	3·44	0·25	1·10	21·97	78·03	12·73
Talavera wheat from Hohenheim	2·59	0·18	2·80	16·54	80·78	15·43
Whittington wheat from do.	2·68	0·19	3·13	17·11	78·58	13·93
Sandomier wheat from do.	2·69	0·19	2·40	17·18	78·89	15·48
Rye-flour from Vienna, No. 1	1·87	0·13	1·33	11·94	85·65	13·78
" " No. 2	2·93	0·21	1·07	18·71	78·97	14·68
Rye (Staudenroggen) from Hohenheim	2·78	0·15	0·86	17·75	80·86	13·94
Rye (Schilfroggen) from do.	2·47	0·18	2·37	15·77	82·67	13·82
Polenta-meal from Vienna	2·14	0·15	0·86	13·66	84·90	13·36
Indian corn from Hohenheim	2·30	0·16	1·92	14·68	84·52	14·96
One-grained wheat from Giessen...	2·07	0·15	2·01	13·22	84·52	14·40
Barley from Hohenheim	2·31	0·16	2·84	14·74	84·80	16·79
Common winter barley from do.	2·79	0·20	5·52	17·81	80·64	13·80
Kamschatka oats from do.	2·39	0·17	3·26	15·26	86·05	12·71
Early white oats from do.	2·82	0·20	4·14	18·00	83·08	12·94
Common rice	1·16	0·08	0·36	7·40	91·60	15·14
Buckwheat flour from Vienna	1·08	0·07	1·09	6·89	91·52	15·12
Tartar buckwheat from Hohenheim	1·56	0·11	2·30	9·96	90·38	14·19
Green peas from Vienna	4·42	0·14	3·18	28·02	67·31	13·43
Field peas from Giessen	4·57	0·14	2·79	29·18	66·23	19·50
Table beans from Vienna	4·47	0·14	4·38	28·54	66·70	13·41
Large white beans from do.	4·59	0·14	4·01	29·31	66·17	15·80
Lentils from do.	4·77	0·15	2·60	30·46	65·06	13·01
White potatoes from Giessen	1·56	0·11	3·61	9·96	86·36	74·95
Blue potatoes do.	1·20	0·08	3·36	7·66	88·20	68·94
Carrots do.	1·67	0·12	5·77	10·66	84·59	86·10
Beet-root do.	2·43	0·17	6·43	15·50	73·18	81·61
Radishes do.	1·81	0·13	5·02	11·56	78·49	82·25
Yellow turnips do.	1·45	0·10	4·01	9·25	90·32	83·28
Turnip-rooted cabbage do.	1·98	0·14	7·02	12·64	81·33	87·78
Onions	1·18	—	8·53	7·53	—	93·78

The numbers of the non-nitrogenous substances, given in the fifth column, refer not only to the starch, but include, in addition to this, the cellulose, wax, or fat, &c.; and hence it was important to determine directly the starch contained in these substances. Krocker made determinations of this kind, which yielded the following numbers for every 100 parts of the dried substance :—

	Parts of starch.	
Pure starch from beans	99·96	—
Wheat-flour, No. 1	65·21	66·16
" No. 2	66·93	67·42
" No. 3	57·70	57·21
Talavera wheat	55·92	56·59
Whittington wheat	53·06	51·84
Sandomier wheat	53·83	52·92
Rye-meal, No. 1	61·26	60·56
" No. 2	54·84	54·12
" No. 3	57·07	57·77
Rye (Staudenroggen)	44·39	44·80
" (Schilfroggen)	47·71	47·13
Meadow oats	37·93	36·90
Kamschatka oats...	39·55	40·17
Barley meal	64·63	64·18
Barley	38·62	37·99
Jerusalem barley...	42·66	42·03
Buckwheat flour	65·05	—
Buckwheat	43·80	44·45
Indian meal	77·74	—
Indian corn	65·88	66·80
One-eared corn	55·51	53·76
Rice	85·76	86·63
Beans	37·71	37·79
Peas	38·81	38·70
Lentils	39·62	40·08

From these and several similar determinations Liebig* has constructed a table, which affords a general view of the proportion between albuminates and non-nitrogenous nutrient substances in the most common articles of food for man (taking the albuminates as the unit). As Liebig here considers the non-nitrogenous matters mainly as promoters of animal heat, and as these bodies, namely the fats and carbo-hydrates, exercise a different influence on the generation of heat, according to the amount of oxygen which they contain, it is necessary for the simplification of the proportion to take their amounts of oxygen as the measures of comparison between the fats and carbo-hydrates; ten parts of fat must thus in reference to the generation of heat correspond to about 24 parts of starch; sugar of milk and glucose are thus naturally reduced to the corresponding value of starch by the deduction of the water. On this supposition *the relation of weight between the plastic and the non-nitrogenous constituents of the food* is as follows:—

	Plastic.		Non-nitrogenous.		
In cows' milk	10	:	30	=	8·8 fat. 10·4 milk-sugar.
„ woman's milk	10	:	40		
„ lentils	10	:	21		
„ horse beans	10	:	22		
„ peas	10	:	23		
„ fat mutton	10	:	27	=	11·25 fat.
„ fat pork	10	:	30	=	12·50 „
„ beef	10	:	17	=	7·08 „
„ hare	10	:	2	=	0·83 „
„ veal	10	:	1	=	0·41 „
„ wheat-flour	10	:	46		
„ oatmeal	10	:	50		
„ rye-meal	10	:	57		
„ barley	10	:	57		
„ white potatoes	10	:	86		
„ blue do.	10	:	115		
„ rice	10	:	123		
„ buckwheat meal	10	:	130		

Anderson† has recently made very extended analyses in reference to the nutrient qualities of different kinds of fodder for cattle.

If we refer to what has already been stated in the general consideration of the metamorphosis of animal matter regarding the physiological importance of the separate groups of nutrient substances generally, and of that of the fats and carbo-hydrates specially, we shall be induced to distinguish articles of food according to the quantity of fat and carbo-hydrates which they contain;

* Chem. Briefe. 3 Aufl. 1851, S. 463, [or Letters on Chemistry. London, 1851, p. 361].

† Journal of Agriculture, 1853, p. 508–518.

that is to say, the relatively best kinds of food must contain fat as well as carbo-hydrates; under favourable relations the animal body is certainly able to elaborate from the carbo-hydrates the fat which it requires; but independently of the fact, that this production of fat would appear from all our positive experiments to be tolerably limited, the production of sugar in the animal organism shows, that fat and sugar have very different and not unimportant objects to fulfil in it (see p. 220). If it be true that the dictates of animal instinct ought in general to be followed, this is more especially the case in reference to the selection of food. The general disposition to combine highly amylaceous food with fats, and fatty matters with amylaceous substances, and the undoubted greater digestibility of such mixtures, prove no less than the simultaneous occurrence of fat and sugar in the milk of animals, which is generally recognised as a normal type of food, that both substances are necessary to the completion of an article of nourishment which perfectly satisfies the requirements of the animal organism. If, therefore, any one of these substances may serve in certain general relations as a substitute for another, especially in reference to the development of heat, this does not in any way militate against the special utility of either. But when Liebig included such different substances as fats and carbo-hydrates under the general designation of respiratory elements, he was far from holding the opinion that, independently of the difference in their capacity for generating heat or their so-called respiratory value, they were of equal importance in the metamorphosis of animal matters—a fact of which we might readily convince ourselves by an attentive study of his most recent deductions regarding the forms of metamorphosis which the fats and sugar undergo. Although Liebig compares animals to "moving furnances" in respect to the development of heat and its causes in the animal body, it requires a strong faith to interpret this expression in the broadest sense of the words, or to regard his somewhat overstrained physical view as calling for serious refutation. Liebig ranks the fats with the carbo-hydrates in his consideration of the different articles of food, on the one hand, because both serve to compensate for the carbon and hydrogen which are lost through the lungs, and on the other hand, because however much might be advanced in favour of a systematic separation of these groups, their specific functions in the metamorphosis of animal matter have not been determined with sufficient strictness either by decided experiments or direct observation. The time, however, will come, and is assuredly not far distant, when we

shall be able by establishing the relations of the most favourable admixture of different articles of food, to keep the fats and carbohydrates sufficiently separate, and to attempt to ascertain the proportion between each individual element of nutrition and all the others. For the present we must take the normal food which nature itself has prepared for the infant organism as the standard by which to judge of the most favourable proportions in the mixture of nutrient substances. If we assume the mean constitution of woman's milk to be that mixture of the four groups of substances which is best adapted for the nourishment of the human organism, we should find that the most nutritious food exhibits the proportion of 10 parts of plastic matter, 10 parts of fat, 20 parts of sugar, and 0·6 of a part of salts.

In our investigation of the most favourable mixture of the different nutritive matters, we must not forget that these relations change in accordance with the condition of the organism, for the requirements of the body equally demand variations in the composition of the food and in its absolute quantity. Even in the consideration of milk, we are struck by the fact, that nature has been careful to vary its composition in accordance with different circumstances, whilst its proportions remain invariably the same under perfectly similar circumstances. The proportion of the constituents of this nutrient fluid, which nature provides for the suckling which has just begun to breathe, is the same in every case, but is quite different from that which is supplied to young animals after they have breathed the air for a longer time. The proportions in which the constituents of the milk occur are moreover different for the different classes of animals; cows' milk contains relatively less sugar and more fat and casein than woman's milk; while asses' milk contains very little casein, but, on the other hand, much sugar and far more fat. It cannot be denied that (as we have already noticed in vol. ii, p. 337) the food which the mother may happen to take exerts a certain influence on the proportion of the constituents of the milk; but it may be readily shown by a comparison of the investigations made in relation to this subject, that there is for every species of animal a certain fixed proportion between the constituents of this primary food. It would appear obvious from these indications, that the requirements of the animal organism, which are influenced by various more or less preponderating agencies, must present differences in the admixture of the necessary nutrient matters. The effect of different influences of the external world, the higher or lower excitation of the individual

animal functions, mental excitement, &c, necessarily call for a restoration of the material parts lost in the different processes. This is so clear that there can scarcely be a doubt on the subject; but we are still entirely in the dark in reference to the more exact determinations of the proportions which are required to enable us to calculate the composition of the food, which is best adapted for each special organism. The physiologist should, however, attempt to calculate for a given organism under certain definite conditions, the proportion in which the special nutrient matters ought to be mixed in order that the persistent well-being of the organism may be secured; and in this respect physiology has the best prospect of attaining to determinate numerical values; from these we may then construct general formulæ, by means of which we may be enabled to predict with mathematical certainty the result of any definite action upon the animal organism. The functions which must be considered in a formula of this kind are certainly very numerous, and very many investigations have still to be made before this object can be attained. But if this be an extensive field whose cultivation is still beset with great difficulties, it yet promises the richest results which may not only influence theory, but which will also make a marked impression upon practical life. Dietetics would then be based upon a firmer foundation, and it will no longer remain a mere illusive idea that the healing art may be made accessible to exact inquiry.

A more important question than the determination of the relations of mixture in different articles of nutrition is that of the absolute quantities of food which are requisite for the maintenance of life, and for the energetic accomplishment of all its functions. A very great number of observations which contribute towards the solution of this question have been made on man as well as on animals. These investigations have, however, been conducted rather with the view of comparing together the excreta of the animal organism generally, and of finding some standard for the amount of the metamorphosis of animal matter, than with special reference to the question of the quantities of favourably mixed food, which the organism requires for its natural well-being. If for the present we put these investigations entirely out of the question, and consider the methods by which we may determine the amount of food which is necessary to the organism, we find that there are two modes of determination which especially present themselves to our notice. The first method consists in experimenting upon oneself or upon animals with the smallest possible quantities of differently

mixed food, until we have been able to find the suitable amount and the most correct proportion for each individual case; but this mode of testing could only be adopted at the expense of trouble and time, and would throw little or no light on the question. We must, therefore, look about us for some guide in this method of inquiry, and this we shall find in the investigation and quantitative determination of the excretions of the animal body. If the latter actually afford a standard for the metamorphosis of animal matter, and if we are able, from their quantity and composition, to judge of the true loss which the animal body experiences during the activity of its organs, they ought also to give us the quantity and quality of those substances, which the organism requires for the restoration of its effete matters. This last method of inquiry, which is based upon the proposition that the requirements of nutrition are regulated by the amount of the loss in the body, appears at first sight to be so simple that one might almost wonder why, after such labours as those of Boussingault, Liebig, Valentin, Barral and other distinguished investigators, this problem has not yet been completely solved; but the inquiry is here met by numerous difficulties which have hitherto prevented any exact determination even for the simplest relations, partly on account of the constant fluctuations in vital activity and partly from those external influences which do not admit of calculation but which materially affect inquiries of this nature. In order to simplify the observation, we should be especially carefully to see that the organism which was made the object of investigation did not present any increase of weight in its organs, or that it was no longer at that period of growth, during which it required to consume more materials than could be again traced in the excretions; we must further avoid that kind of feeding to which the term "fattening" is applied in agriculture; in short, the organism should be maintained in all respects in its normal state, in order that a conclusive proof may be drawn from the excreta in reference to the necessary amount of food. The best method, therefore, of finding at least the minimum of the food necessary for the support of life, is after stopping all supplies from without, to determine the quantities of matters which the organism loses by the excretion of urine, fæces, and products of perspiration. The numerous experiments on inanition, which were formerly made on different animals, appeared to present a good basis for this mode of observation. But, however important it may be to know the minimum quantities needed for the continuance of the life of the organism, these kinds of expe-

riments afford very slight indications of the quantities of food which are necessary to maintain the animal in perfect health and in the full use of its powers. When we deprive an animal of all food, all its functions become impaired, both in their intensity and extent; and abnormal symptoms frequently occur, such as diarrhœa, stases of blood in the different systems of capillaries, &c.; if, therefore, we wish to make the excretions of such animals a measure by which to judge of the quantity of food indispensable to life, we must remember that this measure would scarcely suffice to afford the organism more than a scanty existence, for, as we have already stated, the functions of the organs, the manifestations of force, and the metamorphosis of matter connected with it, are totally different in a state of repletion and in inanition. Such experiments are nevertheless of high value to science.

But how can the smallest quantity be discovered for an amount of food which may give the organism the full use of its faculties? If the absorption of nutrient matters in the intestine, that is to say, the absorption of digested matters were limited to a greater extent than it really is, if no more nutrient matters entered the blood than were necessary for the reproduction of the tissues and of the various functions, we might, perhaps, notwithstanding some difficulties, calculate with tolerable exactness the amount of food required for the organism, from a comparison of the excretions and the food which had passed unchanged into the fæces. Now we know, from our previous considerations, that the organism is not able to convert an unlimited quantity of nutrient matter into blood; we always found that after partaking abundantly of any kind of nutrient substance, some portion of it remained unchanged. The exact determinations by weight, made by Boussingault in reference to fat, those of Bidder and Schmidt in reference to the albuminates, and those of von Becker in reference to the carbo-hydrates, prove that only definite quantities of these substances can be resorbed by the intestine within a certain period of time. But nature has also here given very wide limits to animal motions; thus, for instance, very many experiments show that the organism is able to absorb through the intestinal capillaries and the lymphatics a much larger amount of nutrient matter or chyle, than it requires for the restitution of the effete substances, or for the accomplishment of different purposes of life. In overfeeding the animal which is being experimented upon, a part of the food certainly passes unchanged into the excrements, but another portion enters as superfluous nutrient matter into the blood, where it is

not employed either for the restoration of lost materials, or for the increase of mass in the body or its individual organs, or for the accomplishments of any other objects of life, but is again given to the external world, after having undergone certain alterations which render it more capable of being excreted. There is, therefore, an actual superfluous consumption (*Luxus-consumption,* to use C. Schmidt's expression), whenever there is this abundant supply of food. In such a case the organism takes up far more than it requires even for the most active accomplishment of all the vital functions. The difficulty consists, therefore, simply in this, that we are unable accurately to determine the mean which will give the organism neither too little nor too much nourishment for the maintenance in their normal equilibrium of all the movements of matter, and the manifestations of force depending upon them. Schmidt and Bidder have, therefore, designated as superfluous consumption (*Luxus-consumption*) whatever exceeded the amount of food which was shown in experiments upon fasting animals to be absolutely necessary to life; and hence they have taken the minimum value of the metamorphosis of matter, as the unit with which all further experiments on nutrition might be compared.

In determining the absolute quantities of the nutrient substances, on which the metamorphosis of matter depends, there are three magnitudes which we are especially called upon to consider: the first is the quantity of food which will prevent the organism from sinking by starvation; the second is that which affords the right supply of nourishment for the perfect accomplishment of the vital functions; and the last is that which indicates the sum of nutrient matter which may under the most favourable circumstances be subjected to metamorphosis in the blood.

If we should succeed in ascertaining the mean amount of the metamorphosis of matter, and consequently of determining the corresponding quantity of food, it would be very readily seen, that like everything in the living organism, this amount will also vary excessively according to existing conditions. It appears almost self-evident that there should be a greater consumption when all the vital functions are in a state of unwonted energy, or during any considerable or continuous manifestation of force, than in a state of rest or vegetative passivity; the previously noticed increase of the urinary constituents, and the more profuse perspiration after bodily exertion, have afforded the most positive proof of this fact. The necessity for nourishment is, therefore, increased with the increase of external activity (activity dependent on exertion); this

proposition is so clear, and is proved by such numerous facts in our daily experience, that it would be superfluous to enter more fully into this subject; we will only observe that in addition to the above-indicated standard, a special standard might also be established for the consumption required during a period of bodily labour, and that, in addition to these, many other relations involve differences in the requirements of nutrition.

In all these cases, we have proceeded on the assumption that we are considering an organism which has attained its full development,—in which, therefore, the absolute weight of the living object remains the same, so that the excreta can be accurately balanced by the ingesta. There is still greater difficulty in deciding the question regarding the absolute extent of the requirements of nutrition when growth, corpulence, or pregnancy, and similar relations in which there is an increase of weight, have to be considered; in these cases the excreta fall below the ingesta, and hence the latter cannot furnish any conclusions regarding the quantity of the nutrient matters which are necessary for the due accomplishment of these physiological functions. Boussingault was here as throughout the whole of this department of inquiry, the first to lead the way, and he instituted a numerous series of investigations which have already yielded the most brilliant results. Yet notwithstanding all these investigations we have hitherto failed in establishing any sharply defined determinations of the amount of food necessary to the organism under certain given relations. However much we may have learnt from the laborious researches of different inquirers, we are still entirely wanting in the exact normal determinations, to which we had hoped to attain in this department of science.

The sketch which we have here given of the experiments made to determine the necessary amount of food could only serve as an introduction to further considerations of the actual phenomena of nutrition; while at the same time it might indicate the direction by which we might most securely traverse the still mysterious labyrinth of ever varying phenomena. It might not be out of place if, before we passed to the special statistics of the metamorphosis of animal matter, we were once more to revert to the limit which the resorption of nutrient matters from the intestine cannot exceed, and which consequently appertain to nutrition and the metamorphosis of matter. Although this subject has frequently been touched upon in the course of this work, we have deferred to the present moment entering more fully into this question, as it has the most

direct bearing upon the phenomena of nutrition, which we are about to consider, its elucidation being to a certain extent the first point from which we are able to obtain an insight into the quantitative relations of the metamorphosis of matter during nutrition. Unfortunately, however, we possess only very imperfect investigations on this subject, the most complete of which are those which were made by Boussingault* on ducks. These animals were left without food for 36 hours before the beginning of each experiment, although they were allowed to take water during this time; for the purpose of the actual experiment the food in question was introduced in the form of balls; the ducks were killed at different intervals of time, and the excrements, as well as the contents of the intestines were analysed with special reference to the quantity of fat and nutrient matters still remaining unresorbed. It was of course necessary to determine before each series of experiments the quantity of fat and of other matters, which generally remained in the intestine even after 36 hours' fasting. However carefully these investigations may be conducted, we ought to exercise considerable caution in deducing any conclusions from the results thus obtained. For independently of the fact, that these results obtained from ducks do not admit of comparison with the corresponding relations of higher animals, the birds thus experimented upon not only obtained the articles of food given to them, unmixed with other substances, but also in a form to which they were entirely unaccustomed. We have already seen under the head of "Digestion," that individual articles of food, as for instance, the nitrogenous matters, when they are introduced into the intestinal canal independently of other substances, are less easily digested; there would, therefore, be less matter to be resorbed in these cases than usually occurs under the ordinary relations of nutrition in ducks. Nor can any one deny, that food differing so much from the ordinary kind, as rolled up pieces of dry cheese or gelatin, must be quite inadequate to afford any conclusive evidence of the normal relations of nutrition in ducks. If, however, all these objections were obviated, and the contents of the intestine and the excrements were not only weighed, but also analysed, the circumstance that the intestinal excretion was different during digestion from what it was in a state of fasting, must essentially influence the accuracy of the results; for we know, and shall have still further occasion to see in the course of our considerations, that something more than the undigested and indigestible remains of the nutrient

* Ann. de Chim. et de Phys. 3 Sér., T. 18, p. 444–478.

substances passes into the intestinal excrements, for although we have learnt that far less bile passes into the excrements than was formerly supposed to be the case, we have seen that the intestinal excretion is by no means inconsiderable for certain substances. A far smaller quantity of bile and intestinal mucus is, however, secreted in a fasting state than in a condition of repletion. Yet notwithstanding these uncertainties, Boussingault's results retain their value, for if we were not possessed of these direct determinations, we should scarcely be able to obtain even an approximately correct idea of these relations. We have, therefore, simply given in the following table the results obtained by Boussingault's investigations, according to which the different substances pass in one hour, in the quantities indicated, from the intestinal canal into the blood of a duck.

	Grammes.	Grammes.	Grammes.
Dry rice (8·68% of albumen and 89·2% of starch)	= 4·20	(= 0·34 of albumen and	3·86 of starch).
Dry cheese (70·69% of fat)	= 2·50	(= 1·93 of casein and	0·57 of fat).
Bacon (96·3% of fat)	= 0·88	(= 0·84 of fat).	
Cacao seed (48·4% of fat)	= 1·77	(= 0·84 of fat).	
Starch	= 5·26		
Sugar	= 5·62		
Boiled white of egg	= 1·25		
Casein (anhydrous)	= 1·37		
Gelatin (anhydrous)	= 4·40		
Beef (boiled, free from fat)	= 1·41		
Albumen and gelatin (649 : 3000)	= 5·18	(= 0·92 of albumen and	4·26 of gelatin).

In connection with these uncertain determinations, several highly interesting considerations here suggest themselves, to which we shall revert at a future page; contenting ourselves for the present with the observation, that the albuminous substances alone are totally insufficient for the restoration to the body of the carbon which is lost by respiration; according to Boussingault, a duck expires in one hour 1·25 grammes of carbon, whilst the albuminates which are resorbed within an hour contain at most only 1·0 gramme of carbon. Fats or carbo-hydrates must, therefore, necessarily be commingled with the albuminates, in order that there may be a due compensation in the body for the loss of carbon which normally occurs through the respiration. It is still more striking, that the quantity of fat which is resorbed in one hour should be wholly inadequate for this restitution of the carbon; 0·84 of a gramme of fat, which is all that is resorbed during one hour, contains about 0·7 of a gramme of carbon, and, therefore, scarcely half as much as is exhaled by the lungs in one hour. The carbo-hydrates are, how-

ever, resorbed by the intestine in sufficient quantities for the requirements of respiration, and it is moreover worthy of notice, that very nearly as much carbon is introduced into the body in equal periods of time by starch as by the absorbed sugar. (For 5·26 parts of starch and 5·62 parts of sugar which are resorbed in one hour, both contain about 2·37 of carbon.)

The very important question here presents itself, as to what changes are impressed upon the blood in consequence of the absorption of different nutrient matters; this being undoubtedly the first step we ought to take if we would enter upon the investigation of the nutrition of the animal body. Yet notwithstanding the efforts of numerous admirable investigators, we are still very imperfectly acquainted with the most important points of this inquiry. We have already referred to the influence which nutrition in general or digestion exerts on the physical and chemical characters of the blood (see vol. ii, p. 261). Very few special investigations, deserving of notice, were made in reference to the influence of different kinds of food on the constitution of the blood before those of H. Nasse,* with which we may associate an observation of Verdeil † on the ash of the blood of one and the same dog, which had been fed both on animal and vegetable diet. The relative quantity of chloride of sodium was in both cases nearly the same (50%); after the dog had been fed upon animal food the ash contained more sulphuric and phosphoric acids, and considerably more soda and oxide of iron, but somewhat less potash, and very much less magnesia than after a vegetable diet. Boussingault ‡ was as little able as Bouchardat and Sandras to discover that fatty food had any decided influence on the amount of fat in the blood of dogs.

Notwithstanding the numerous experiments which have been made by Nasse, the number of constant results which they have yielded is relatively very small, in consequence of the great fluctuations which were observed in the constitution of the blood; these results reduce themselves to the following points: after a meat diet the blood-corpuscles in the dog exhibit a greater capacity for sinking; the blood itself presents a darker colour, which becomes whitish after the abundant use of fat; the coagulation occurs somewhat more rapidly than on a vegetable diet; a continuous animal

* Ueber den Einfluss der Nahrung auf das Blut. Leipzig, 1850.

† Ann. d. Ch. u. Pharm. Bd. 69, S. 89-99.

‡ Ann. de Chim. et de Phys. 3 Sér., T. 24, p. 460-464.

diet increases the amount of fibrin (as I have observed* in my own case,) after living exclusively on purely animal food, and augments the amount of the phosphates and of the salts generally. The quantity of fat in the blood increases even during the first hour after the use of food which is rich in fat; but it speedily falls again.

The blood of dogs is for the most part of a somewhat lighter shade of colour when kept on vegetable than when kept on animal food, and the sinking capacity of the blood-corpuscles is somewhat smaller; the specific gravity of the blood, as well as that of the serum, is increased during the first five hours by a vegetable diet (especially if this be combined with the simultaneous use of sugar). The amount of fibrin is not altered; the fat, however, is somewhat diminished, whilst the amount of the salts including that of the phosphates is somewhat lessened.

Continuous deprivation of food renders the blood somewhat paler in colour, retards its coagulation, and raises the specific gravity both of the blood and of the serum; the number of the blood-corpuscles is very fluctuating; the fibrin rises only slightly; while the amount of the salts is very considerably increased.

After the last meal the quantity of the solid constituents of the blood increases to the ninth hour, when it again begins to sink.

The few results which Nasse has been able to deduce from the careful labours which he prosecuted for years, show how unable we still are to trace the metamorphosis of the nutrient matters in nutrition through its individual phases. We have here a confirmation of the remarks which we made in our introduction, that our knowledge of the internal metamorphosis of matter is still extremely incomplete, and that it is only by a comparison of the chemical qualities of the different juices and tissues, and more especially by carefully conducted statistics of the final results of the metamorphosis of animal matter, that we can hope to form a correct judgment or arrive at anything like conclusive views. We cannot, therefore, trace in detail the final destinies to which the albuminates, the fats, the carbo-hydrates, and the salts are subjected in the animal body, nor can we venture to do more than indicate the facts that lead us to those considerations, which we have already given in relation to the metamorphosis of matter generally (see p. 207). It, therefore, only remains for us to notice, in reference

* Journ. f. pr. Ch. Bd. 27, S. 16.

to the chemical phenomena of nutrition, the facts and the conclusions to be deduced from them, which have hitherto been obtained from statistical investigations.

The next question which must engage our attention in this respect, is to determine the amount of food which, under normal relations, is daily subjected to the metamorphosis of matter in an adult man, and the mode in which the products, into which the nutrient matters are decomposed during their stay in the body, are distributed in the excretions. The earliest exact investigations of this kind were made by Valentin* on his own person. His bodily weight being 53 kilogrammes, Valentin found that he consumed in the twenty-four hours on an average 2924·03 grammes of mixed food; of the products of metamorphosis which were excreted during that time 190·73 grammes were eliminated with the solid excrements, 2447·70 grammes with the urine, and 1246·93 grammes with the perspiration; the ratio of the solid and fluid to the gaseous excretions is, therefore, on an average as 1 : 0·833. This estimate seems tolerably high for the perspiration; but it appears from Valentin's special investigations, that the main factor which raises the amount eliminated by the perspiration is especially the separation of water through the skin, on which account this proportion must be totally different in animals.

The experiments of Rawitz,† which were conducted with great patience and self-sacrifice, still leave much to be desired in reference to their exactness; the mean of twenty-two observations, in which he studied the effect of many of the most common articles of food, yielded on an average, for a consumption of 1875·4 grammes of mixed food, 1136·4 grammes of egesta through the intestine and kidneys, and 739·0 through the perspiration; the ratio given by Rawitz of the solid and fluid to the gaseous egesta differs, therefore, very considerably from that of Valentin, being as 1 : 0·650; the ratio in his individual observations was extremely fluctuating, as was also the case with Valentin.

Rigg ‡ determined the ingesta and egesta of a strong man, in accordance with their elementary constituents; he obtained results which accorded tolerably well with those of other observers: it is however remarkable, that for 100 parts of the nitrogen which was

* Valentin's Repert. 8. Jahrg; Handwörterbuch der Physiologie. Bd. 1, S. 367-470; and. Physiol. d. Menschen. Bd. 1, S. 710-780.

† Ueber die einfachen Nahrungsmittel. Berlin, 1842.

‡ Medical Times, 1842, p. 278.

absorbed in these experiments (which were prolonged for twelve days) only 50·8 parts passed into the urine.

The following observation, in reference to the excretion of nitrogen, was made by myself,* on my own person: during a purely animal diet (eggs), I took daily on an average 30·3 grammes of nitrogen, and discharged 24·4 grammes by the urine; hence five-sixths of the absorbed nitrogen were again given off through the kidneys.

The best investigation of the statistico-chemical relations of the quantitative metamorphosis of matter in the animal organism, which has as yet been made, is due to Barral,† who, however, has merely taken into account the elements of nutrition and of the excretions. He made five series of observations, two on himself, (when at the age of twenty-nine years, the one in winter and the other in summer) one upon a boy aged six years, the fourth upon a man whose age was fifty-nine years, and the fifth upon a woman aged thirty-two years. The combined results of this investigation were as follows:—

	Daily absolute quantity in grammes.						
	Ingesta.			Egesta.			
	Fluid and solid food.	Oxygen.	Sum.	Perspired water.	Carbonic acid.	Solid and fluid excretions.	Other losses.
Man, aged 29 years, in winter ...	2755·0	1061·5	3816·5	1287·8	1230·9	1265·0	32·8
„ „ in summer ...	2386·0	777·3	3163·3	1141·6	888·4	1099·4	33·9
Boy, aged 6 years	1396·2	423·4	1819·6	694·7	514·0	604·6	6·3
Man, aged 59 years	2710·7	889·1	3599·8	522·6	1088·3	1962·8	26·1
Woman, aged 32 years	2339·6	886·7	3226·3	998·7	1006·9	1191·6	29·1

For a healthy adult man the egesta, corresponding to 100 grammes of ingesta (that is to say, 73·8 grammes of food, in which there were 18·56 parts of solid matters and 55·24 parts of water, and 26·2 parts of oxygen), would be distributed in the following manner, namely: 34·95 grammes of water and 30·55 grammes of carbonic acid would be eliminated by the lungs and skin, 33·95

* Journ. f. pr. Ch. Bd. 27, S. 258.

† Compt. rend. T. 27, p. 361, and Ann. de Chim. et de Phys. 3 Sér., T. 25, p. 129-171.

grammes as urine and fæces, and 0·55 of a gramme through other channels.

If we calculate from Barral's experiments the distribution which 100 grammes of absorbed carbon undergo in its excretion after it has fulfilled its functions in the organism, we shall find that (in an adult man) 91·59 grammes pass into the products of perspiration, and only 4·58 grammes into the urine, and 3·83 grammes into the fæces. According to this estimate, more than nine-tenths of the carbon contained in the food are entirely consumed and converted into carbonic acid.

If we pursue a similar method of inquiry in reference to the mode of excretion of nitrogen, and follow the experiments which Barral instituted on his own person, we arrive at the following results: (the nitrogen in the food taken by Barral being to the carbon as 1 : 12·8 ;) for every 100 parts of absorbed nitrogen only 8·33 parts were again excreted with the fæces, while 42·07 parts were given off with the urine, and 49·6 parts through the skin and lungs. The relative amount of the nitrogen eliminated by the perspiration is here excessively large, and entirely at variance with the experiments which many other investigators have made on animals.

It further appears from the above table, that for every three parts by weight of solid and fluid food (that is to say, such food as Barral used during the prosecution of his experiments, and which consisted on an average of 25·15% of solid substances), about one part by weight of oxygen entered into the metamorphosis of matter. The water which was separated through the lungs and skin amounted in all the cases (excepting that of the man aged fifty-nine years,) to somewhat more than the quantity which was discharged by the sensible excretions. It follows, moreover, from these experiments, that an adult man oxidises on an average 289·0 grammes of carbon, and 18·6 grammes of hydrogen, in the twenty-four hours.

However carefully these investigations may appear to have been conducted, they yet can only serve as examples of the manner in which the consumption of matter occurs under different relations in the human organism; but as very many conditions which exert an essential influence on vegetative life must be wholly disregarded, and as, moreover, the method of investigation does not exclude all doubt of the accuracy of the results even in special cases, these very meritorious labours can scarcely for these reasons, and in consequence of their isolated character, be of any great ser-

vice to science, or furnish any fixed points of support for more extended conclusions. As was naturally to be expected, the comprehensive experiments on animals, conducted by Valentin and Boussingault, and more recently, and to a still greater extent, by C. Schmidt and Bidder, possess far greater certainty, and afford us a deeper insight into the combined relations of nutrition in the animal organism.

Valentin* prosecuted very careful investigations on the balance of the metamorphosis of matter for three days consecutively on a four-year-old mare. The results of these experiments may be thus summed up. The quantity of the discharged fæces exceeded in this case, by three or four-fold, the quantity of the urine that was excreted; half of all the excreted matters was always carried off by the perspiration, and, consequently, half of the daily food was again eliminated by the lungs and skin during the twenty-four hours. A larger quantity of water was discharged with the fæces than with the urine, and less water was given off by the perspiration than through the urine and excrements. The quantity of water which was daily introduced into the system amounted to one-fourteenth of the mean weight of the body. A larger quantity of organic matter was removed with the fæces than with the urine. Upwards of twice, but considerably less than three times the amount of the organic elements was eliminated by the perspiration. The quantity of organic matter daily consumed amounted to from 1-42nd to 1-43rd of the mean weight of the body; the organic matters eliminated with the fæces ranged from 1-139th to 1-150th of the weight of the body, and those excreted with the urine from 1-208th to 1-209th; and those through the perspiration on an average to 1-62nd of the weight of the body. By far the greater part of the fixed salts was eliminated with the fæces. About 3-10th of the fixed salts taken up with the food are carried off by the perspiration. The sensible excretions consisted on an average of 84·11% of water, 13·76% of organic constituents, and 2·13% of ash; and the perspiration contained 64·28% of water, 34·67% of organic constituents, and 1·05% of ash; the food which was daily consumed contained on the other hand 74·75% of water, 23·63% of organic constituents, and 1·62% of ash. The percentage numbers obtained for the food stand between those yielded by the sensible excretions and the perspiration.

Boussingault † made a similar series of experiments on a horse

* Op. cit.

† Ann. de Chim. et de Phys. T. 61, p. 128.

and a cow. From these experiments of Boussingault, Valentin has drawn up the following table in which the total sum of the water, of the ash, and the individual elements of organic matter taken up with the food, is placed in juxta-position with the mean numbers of the daily quantities of water, ash, and organic elements again eliminated through the urine, fæces, and perspiration.

Constituents.	Total sum of the food.	Fæces.	Urine.	Perspiration.
	Grammes.	Grammes.	Grammes.	Grammes.
Water	17364·7	10725·0	1028·0	5611·7
Carbon	3938·0	1364·4	108·7	2465·0
Hydrogen	446·5	179·8	11·5	255·2
Oxygen	3209·2	1328·9	34·1	1846·1
Nitrogen	139·4	77·6	37·8	24·0
Ash	672·2	574·6	109·9	12·3
Sum	25770·0	14250·3	1330·0	10189·7

Hence the elements of the 100 parts of the food consumed by the horse are distributed in the following proportions in the excretions:—

Of 100 parts of		The Fæces.	The Urine.	The Perspiration.
Water	There are given off to	61·8 per cent.	5·9 per cent.	32·3 per cent.
Carbon		34·6 „	2·7 „	62·7 „
Hydrogen		40·3 „	2·5 „	57·2 „
Nitrogen		55·7 „	27·1 „	17·2 „
Oxygen		41·4 „	1·0 „	57·6 „
Ash		85·5 „	16·2 „	—
The food generally		55·3 „	5·2 „	39·5 „

An experiment which was continued for three whole days upon a milch cow yielded the following numbers:

Constituents.	Total amount of the food.	Milk.	Fæces.	Urine.	Perspiration.
	Grammes.	Grammes.	Grammes.	Grammes.	Grammes
Water	71965·0	7388·4	24413·0	7239·2	32924·4
Carbon	4813·4	628·2	1712·0	261·4	2211·8
Hydrogen	595·5	99·0	208·0	25·0	263·5
Oxygen	4034·6	321·0	1508·0	253·7	1951·9
Nitrogen	201·5	46·0	92·0	36·5	27·0
Ash	890·0	56·4	480·0	384·2	30·6
Sum	82500·0	8539·0	28413·0	8200·0	37348·0

For the cow, therefore, every 100 parts of the elements of the food are distributed in the following proportions in the excreta:—

Of 100 parts of		The Milk.	The Fæces.	The Urine.	The Perspiration.
		Per cent.	Per cent.	Per cent.	Per cent.
Water	There pass into	10·2	34·4	10·0	45·8
Carbon		13·0	25·8	5·4	54·2
Hydrogen		16·6	34·9	4·2	55·7
Nitrogen		22·8	45·6	18·1	13·5
Oxygen		7·9	37·4	6·3	48·5
Ash		6·1	53·9	43·1	3·1
The food generally		10·3	34·4	9·9	45·4

It will be unnecessary to consider at the present time the conclusions to be drawn from these experiments, partly because they are self-evident from a mere inspection of the table itself, and partly because we shall revert to them at a future page, when we shall enter upon the consideration of similar experiments.

Valentin has also directed his attention to the distribution of the *salts* in the metamorphosis of matter, for which purpose he instituted a comprehensive series of experiments on a horse. These experiments yielded several interesting results in regard to the resorption of certain mineral substances in the intestine: it was found that lime, phosphoric acid, and the alkaline salts were present in great abundance in the urine (having been absorbed during digestion); but that the magnesia occurred only in very small quantities. In the ash of the excrement the phosphate of magnesia was to the phosphate of lime in an inverse ratio to that which occurred in the food, because 60·23% of the magnesia, which had been absorbed, was again eliminated with the solid excrements, whilst only about 25% of the absorbed lime was again given off with the fæces. (Hence arise the frequent intestinal concretions observed in herbivorous animals.)

A mare whose weight was 935 lbs., and her age four years, consumed daily for nutrition and growth, and for other excretions than the fæces and urine, 2·025 ounces of lime, 0·125 of an ounce of magnesia, 0·74 of an ounce of silica, 0·035 of an ounce of chlorine, 0·64 of an ounce of sulphuric acid, 19·25 ounces of phosphoric acid, and 0·76 of an ounce of alkalies. Thus, too, a tolerably large proportion of the silica, which had been contained in the food, could not be again found in the excrements and the urine. Of the

0·3796 of a lb. of the silica which was taken in the ood, 0·0464 of a lb. did not re-appear in the excretions; their application to the formation of the epidermis and hair seems, however, to be proved by the amount of silica which was shown to be present in these parts by Brunner and Valentin as well as by Gorup-Besanez.

Boussingault * made a series of experiments with a view of settling the question whether nitrogen was or was not exhaled through the lungs. These experiments, which were made on turtle-doves fed upon millet, gave the following result for the distribution, through the excrements and the perspiration, of the elements taken with the food. We have calculated the mean of the results of two observations, the one of which extended over five, and the other over seven days.

Of 100 parts of		To the Fæces.	Perspiration.
Carbon	There are given off	20·3 per cent.	79·7 per cent.
Hydrogen		18·7 „	81·3 „
Nitrogen		64·96 „	35·04 „
Oxygen		19·19 „	80·81 „

Sacc† made a perfectly similar series of experiments on fowls which had been fed on barley, at the same time that they had swallowed chalk and sand. These animals (a cock and a hen) had increased 19·18 grammes in weight during the seven days of the experiment; this increase depended upon the assimilation of 12·436 grammes of organic matter and 6·744 grammes of mineral substances; if these are abstracted from the food, we find from Sacc's experiments, that the elements are distributed as follows in the fæces and the perspiration :—

Of 100 parts of		To the Fæces.	Perspiration
Carbon	There are given off	24·5 per cent.	75·5 per cent.
Hydrogen		23·0 „	77·0 „
Nitrogen		42·2 „	57·8 „
Oxygen ...		23·9 „	76·1 „

* Ann. de Chim. et de Phys. 3 Sér. T. 11, p. 433.

† Ann. d. Ch. u. Pharm. Bd. 52, S. 77.

C. Schmidt * has recently, in conjunction with Bidder, prosecuted an inquiry into the relations of nutrition, and these inquiries are distinguished from all previous investigations of this nature by the exactness of the methods employed, the comprehensive determination of all determinable amounts, and the copiousness of the results. These experiments were made on cats and dogs, some of which were abundantly, others sparingly supplied with meat, and others again left for a prolonged time without any food. The nutrient matters and the excretions generally were carefully investigated in reference to their proximate constituents, as well as to the elements which they contained.

We subjoin a table of the distribution of the elements of nutrition in the organism of one of the carnivora, that we may be able to add the results of Schmidt's investigation to the above experiments of other observers; the first series of experiments were made on a full grown cat, weighing 3228 grammes, which had as much meat for a week as it could eat.

Of 100 parts of		To the Fæces.	To the Urine.	To the Perspiration.
Water	There were given off	1·2 per cent.	82·9 per cent.	15·9 per cent.
Carbon		1·2 ,,	9·5 ,,	89·4 ,,
Hydrogen		1·1 ,,	23·2 ,,	75·6 ,,
Nitrogen		0·2 ,,	99·1 ,,	0·7 ,,
Oxygen		0·2 ,,	4·1 ,,	95·7 ,,
Sulphur		50·0 ,,	50·0 ,,	
Salts		92·9 ,,	7·1 ,,	

A comparison between this table and the previous tables, calculated from experiments on herbivorous animals, exhibits very considerable differences in reference to the distribution of the elements in the carnivora and the herbivora; but the most striking feature of this experiment vanishes when we consider that carbon and hydrogen are for the most part conveyed to the latter animals in an indigestible form, and that to a certain extent this is also the case with the nitrogen, which is inclosed in the shape of albuminates in the cells forming the husks of the grain, which are extremely inaccessible to the passage of the digestive fluids.

We at once see that the water is absorbed in much smaller quantity from the intestine in the herbivora than in the carnivora; the difference here is extremely great; in horses and cows, on an

* Verdauungssäfte und Stoffwechsel. S. 289-413.

average, only half of the water which entered the intestine was absorbed, but in the carnivora, as was shown by Schmidt's other experiments, the quantity amounted only to $1\frac{0}{0}$, or at most $4\frac{0}{0}$. If we disregard the quantities of the other elements which remain in the intestine, we find that in the herbivora, a very small portion, from $15\frac{0}{0}$ to $20\frac{0}{0}$ only of the water, which is either absorbed or formed, is eliminated through the kidneys, whilst in the herbivora as much as 4-5ths of the absorbed water passes into the urine. The fact that the absorbed carbon is excreted in far larger quantities through the lungs in the herbivora than the carnivora (the relation of the carbon in the urine being as 1 : 19 in the former, and as 1 : 9·5 in the latter) possibly depends solely upon the nature of the food, and not upon any special relations of the organism; for the non-nitrogenous matters become almost completely decomposed into carbonic acid and water, and hence they yield absolutely nothing, or only a very small amount to the urine, whilst the products of decomposition which are produced from the albuminates yield their nitrogen to the urine, although always in combination with certain quantities of carbon. We thus obtain a kind of check for our calculations of the urine and respiration. In the same manner we find in reference to the hydrogen that relatively much less is eliminated through the kidneys in the herbivora than in the carnivora. (The ratio of the hydrogen excreted through the urine is to that eliminated through the lungs as 1 : 23·0 in the herbivora, and as 1 : 3·3 in the carnivora.) The case differs in respect to the nitrogen; for the herbivora frequently excrete by perspiration as much as $40\frac{0}{0}$ of the nitrogen they had absorbed, whilst the carnivora scarcely eliminate as much as $1\frac{0}{0}$. Earlier investigations have taught us that the urine of the herbivora is poorer in nitrogen and in urea, the substance in which it is carried off, than that of the carnivora, which (as Schmidt has also observed) is very often scarcely anything more than a saline solution of urea. It would, therefore, almost appear as if the process of oxidation were so far more abundant in the herbivora than the carnivora, that in the organism of the former the albuminates were decomposed even beyond what was necessary for the formatiom of urea; and on this account, the urine of the herbivora is entirely deficient in the earlier product of the disintegration of the albuminates, namely, uric acid.

When the metamorphosis of matter is effected in the organism without any compensation from without, the proportions of the elements of the urine to those of the perspiration are almost

exactly the same as in feeding with fat meat, and hence, for the sake of brevity, we shall omit all further details.

If we pause for a moment in our consideration of the excretion of the elements, we shall find the most decisive confirmation, in two interesting series of experiments by Schmidt, of the proposition first enounced by Liebig, that the bile is not only resorbed in the intestine, but is also consumed, and for the most part separated through the lungs. Thus, for instance, we find from the statistical observations made by Schmidt on two dogs, having biliary fistulæ, that whether the animals had had a very abundant or only a scanty flesh-diet, from 10% to 12% of the absorbed carbon, and from 11% to 13₀ of the absorbed hydrogen were excreted by the bile, and that this loss was not uniformly distributed through the excretions, but was exclusively limited to the products of respiration. Only 3% or 3·2% of the absorbed nitrogen passes into the bile, and this is as nearly as possible the quantity which is missing from the urine.

We regret that we are compelled to deviate from our general rule in respect to this comprehensive inquiry, by omitting to confirm by numerical data the facts and conclusions that have been advanced; but had we done otherwise we should have been obliged to transcribe the whole of Schmidt's observations, as he has merely given the most necessary empirical results. We must, therefore, content ourselves with giving the most important conclusions deduced from his inquiries, more especially as many points referring to the individual factors of the metamorphosis of matter would have been introduced in the proper place, had we been earlier acquainted with the special details of these admirable labours.

We learn from the experiments on cats, that for 1000 grammes' weight of these animals there are required in the twenty-four hours at least as much as 44·118 grammes of flesh to maintain the original bodily weight, and that in addition to this, 18·632 grammes of oxygen must be absorbed in order to apply this nutrient matter to the wants of the organism; and, consequently, that the minimum of food for the carnivorous animals experimented-upon averages, according to this observation about 1-23rd, and the necessary oxygen about 1-55th of the whole weight of the body. On the other hand, when the animals are kept without food, only 22·118 grammes are lost in the course of twenty-four hours from the whole weight of the body by the excretions (between the third and the ninth day), to the metamorphosis of which 15·749 grammes of

oxygen are applied; the body loses, therefore, during the first eight days of inanition only about 1-46th part of its weight in the twenty-four hours. But when cats are supplied with as much flesh as they will eat, they are able to absorb such excessively large quantities of it in the metamorphosis of matter, that the flesh they consume amounts to 1-9th, and the oxygen absorbed with it to almost 1-24th part of their bodily weight.

When we compare the products of excretion yielded during a scanty and an abundant supply of flesh, we find that the quantities of the excretions stand in a direct relation to the amount of nourishment, and that, consequently, the increase or diminution of the food exerts no influence whatever on the proportions between the different excreta, or on their quality; the ratio of the absorbed oxygen to that in the exhaled carbonic acid, is in all cases the same, namely as 100 : 79·3. The ratio between the expired carbonic acid and the expired water becomes, however, changed when a larger amount of animal food is taken; thus, for instance, in one case it was found that on a scanty flesh-diet 75·6 parts of aqueous vapour were expired for 100 of carbonic acid, while on an abundant flesh-diet there were only 42·15 parts of water to 100 of carbonic acid; hence in the latter case a relatively larger quantity of water must be separated by the kidneys, as indeed Schmidt's determinations have also shown; for the ratio of the perspired aqueous vapour to the water excreted by the kidneys and fæces is 23·3 : 76·7 in the former, and 17·84 : 82·16 in the latter case. On a scanty flesh-diet, water being at the same time withheld from the animals, the ratio of the carbonic acid to the expired aqueous vapour became so far changed that for 100 parts of carbonic acid 80 parts of water were exhaled by the skin and lungs, and hence in this case there was relatively less water separated by the kidneys than on a scanty flesh-diet without the deprivation of water. These proportions are best seen in the following comparative table which we have calculated from Schmidt's results. We take the flesh that was consumed (that is to say, its dry residue) as the unit, and calculate the amount of solid matters which pass away in the urine and fæces, the perspired carbonic acid and aqueous vapour, but exclude the quantity of water that has been taken and that is separated by the solid and fluid excretions. I. has reference to the metamorphosis of tissue when the minimum quantity of food was taken, there being at the same time free access to water. II. The greatest possible quantity of food and unimpeded access to water. III. A normal flesh-diet (that is to say, one with which the weight of the body remains

constant) without water. These three experiments were made on the same animal, an adult male cat weighing 3200 grammes. IV. has reference to a young cat weighing 1170 grammes which was allowed an excess of flesh and water *ad libitum*.

	I.	II.	III.	IV.
Dried flesh....	100.0	100·0	100·0	100·0
Absorbed oxygen	167·0	166·0	167·3	166·2
Solid residue of the urine	31·3	30·4	30·6	31·4
„ the fæces	1·7	2·5	1·7	2·0
Expired carbonic acid	182·0	181·4	182·6	181·4
„ aqueous vapour	137·6	76·4	152·6	128·7

It is sufficiently obvious from this review that the elementary analysis which flesh taken as food may be regarded as undergoing in the living body, gives in the normal state as accurately defined values as if it underwent a mere process of fermentation or combustion; hence under all conditions, as the above table shows, 1 part of dry flesh is decomposed in the living body with the co-operation of 1·67 parts of oxygen into 0·31 of urinary substances, 0·02 of fæcal matter, and 1·82 of carbonic acid. The conclusions which may be hence drawn regarding the general metamorphosis of matter in the animal body and especially in the carnivora, are too self-evident to require notice.

Since the lean flesh which Schmidt supplied to the cats employed in these experiments, contained 19·56% of albuminates and gelatigenous substances, 4·74% of fat, 1·00% of inorganic matters, and 74·70% of water, while there are contained in the solid residue of the urine, on an average, 85·5% of urea, and 14·5% of salts (containing 2·3% of sulphuric acid), and in the dry solid excrements, on an average 63% of biliary residue, we obtain the following comparative results for 1000 grammes' weight of a carnivorous animal (cats having been employed), if we assume that an animal consumes 50 grammes of fresh lean flesh in twenty-four hours for every kilogramme's weight.

A cat, for every kilogramme's weight, *takes* in 24 hours,	Water.	Albuminates and gelatigenous matters.	Fat.	Salts.
50·000 grammes of flesh	37·350	9·728	2·370	0·510
21·125 „ of oxygen				
71·125 grammes				

A cat, for every kilogramme's weight, *gives off*, in 24 hours,	Water.	Carbonic acid.	Urea.	Salts.	Fæces.	Bile.
39·468 grammes of perspiration...	16·445	23·023	...			
30·761 „ of urine	26·839	...	3·53	0·569		
0·806 „ of fæces	0·681	...	...	0·041		
71·125 grammes.	43·965			0·610	0·039	0·135

We need scarcely observe that the excess of water in the excretions, amounting to 6·615, corresponds to the water which is formed by the process of respiration; the augmentation of the salts is due to the oxidation of sulphur.

While our preceding observations have had reference to the metamorphosis of tissue in full-grown animals, which are undergoing neither an augmentation nor a diminution of their bodily weight, we now proceed to the determination of those relations of nutrition in which either the food is not sufficient to maintain the normal weight of the organism and the energy of its functions, or when an augmentation of the weight of the body, growth or fattening, is going on.

We can here include in a few words all that need be said regarding the conditions which seem to render the nutriment *insufficient* for a given organism, since the consideration of this point necessarily arises from our previous remarks. The nutriment may be insufficient either in its quantity or its composition. We have already attempted, in so far as the present state of our knowledge allows us, to answer somewhat in detail the question regarding the quantity of food that is requisite to retain the organism in its normal state; but we have not entered so fully into the question regarding the quality of the food requisite to keep the body in a thriving condition. Although the subject has been already noticed in the preceding pages, and it might be concluded *à priori* from the facts there laid down, that only such a nutriment could permanently support the integrity of the organism, as contains all the essential elements of food, namely albuminates, fats, carbo-hydrates, and certain salts, it yet remains for us to mention the experiments made by Boussingault, which yield a positive proof of the correctness of these views. Even in what are now considered the older works on physiology we find a description of the experiments of Tiedemann and Gmelin, who failed in keeping geese alive on an abundant diet of white of egg. The experiments made under the direct observation of the Paris Academy on the questionable

nutrient power of bone-gelatin and of gelatigenous tissue, afford us sufficient evidence that this nutrient power cannot be concentrated into a single chemical compound, even if it be of a somewhat complex nature.

Accurate quantitative determinations regarding the influence upon the animal organism of food which is insufficient in quality were first instituted by Boussingault, and were specially conducted in reference to certain agricultural points. We have previously alluded to those experiments of this chemist,* by which he demonstrated the importance of salt for the well-being of the organism—a fact which has been subsequently confirmed by the researches of Plouviez † and Dupasquier.‡ The most decisive conclusions in reference to this subject are however afforded by the investigations which have been carried on by Boussingault,§ Playfair,|| Thomson,¶ Payen and Gasparin,** Persoz†† and others, in reference to the fattening of animals with various kinds of fodder. Since we shall subsequently revert to the influences which most essentially affect the augmentation of the weight (during growth or the process of fattening) we shall here merely give the results (by way of illustration) which Boussingault obtained in his experiments on cows. Potatoes and beet-root alone were insufficient to nourish a cow (that is to say, to retain it at the same bodily weight), even when these kinds of food were supplied to the animal in very great excess. It follows from these, as well as from certain earlier investigations, that every kind of food is insufficient, (1) if it cannot be taken in such large quantities that its nitrogenous matters may serve to replace the organic particles rendered effete by the metamorphosis of tissue, (2) if its digestible constituents do not contain sufficient carbon to supply the carbon which is lost by the respiration and other excretions, (3) if it does not contain sufficient salts, especially phosphates, and, (4) consequently, we find that a certain quantity of fat in the food, notwithstanding the simultaneous presence of carbo-hydrates, if not positively necessary, is yet very desirable in order to retain the organism in a healthy condition.

It seems placed almost beyond doubt, by these experiments,

* Ann. de Chim. et de Phys. 3me Sér. T. 19, pp. 117-123.

† Bullet. de l'Acad. de Méd. T. 14, pp. 1077-1085.

‡ Journ. de Pharm. 3me Sér. T. 9, pp. 309-344.

§ Ann. de Chim. et de Phys. T. 12, p. 153.

|| Philosoph. Magaz. Vol. 22, p. 280.

¶ Trans. Med. Chir. Soc. Vol. 29, pp. 327-340.

** Compt. rend. T. 18, p. 797.

†† Ibid. p. 245.

that the proportions in which these factors of nutrition are mixed in the food exert the most decided influence on the welfare of the organism, and that the intermixture of the different factors of nutrition is essential for the metamorphosis of matter. Great as are the fluctuations which nature allows in these proportions, an undue preponderance of one or other of the factors always acts injuriously upon the due course of the process of nutrition: no single section of this process can go on without the concurrence of all these factors; thus, for instance, all these experiments teach us that the carbo-hydrates alone are not sufficient for the formation of fat in the animal body; in order that fat may be formed, protein-bodies as well as salts must co-operate in the metamorphosis; and it is only by the mutual action of these substances that a formation of fat can possibly take place. Had the results of the above-described experiments been duly considered, such a series of observations as that instituted by Letellier,* who fed turtle-doves on sugar, would hardly have been necessary. Letellier having determined the quantity of fat in doves of equal age, weight, &c., fed similar animals for a long time with sugar; the birds, several of which died after eight days, lost on an average 5·1 grammes, or 3·4% of their bodily weight daily; when a little pure albumen was added to the sugar as food, they died at a somewhat later date, having lost daily 2·3 grammes, or 1·53% of their weight. While the amount of fat in the healthy birds before the commencement of the experiments was 20·88 grammes, or 15%, the amount after death, in those which had been fed on pure sugar, was only 11·3 grammes or 7·36%, and in the case of those which had simultaneously received albumen (and when life was therefore somewhat prolonged) it was only 1·57 grammes or 3·15%. Indeed even after feeding them with butter, the birds sunk, and there was a considerable loss not only in their bodily weight, but even in their fat. (The daily loss of bodily weight was 3·25 grammes or 2·82%, and altogether more than half the original quantity of fat disappeared, there being only 7% after death.) The animals, therefore, sunk in this, as in the other cases, with all the symptoms of inanition, while the process, whose most essential requirements were present, not only failed, but could scarcely be said to have commenced. Hence this proposition, which we previously regarded as resting on many inferences, may be considered to be definitely proved by these experiments.

This consideration directly leads us to the quantitative relations

* Ann. de Chim. et de Phys. T. 11, p. 433.

of the metamorphosis of tissue, when *all solid food is withheld.* In reference to this point we will first mention a series of observations made by Boussingault, which are closely connected with those of Letellier, which we have just described. Boussingault's experiments were also made on turtle-doves, which were kept for seven days without any solid food; they lost daily 4·12% of their bodily weight, and 2·696% (of their weight) of carbon by the respiration, having exhaled daily 3·722% when fed upon millet. The green, bilious-looking, slimy excrements, with which only a few detached white patches of uric acid were mixed, averaged daily, when dried, 0·210% of the weight of the body. The excrements contained 31·95% of carbon, 4·35% of hydrogen, 24·74% of nitrogen, 28·32% of oxygen, and 16·40% of ash. A bird weighing 187 grammes lost, therefore, daily during its starvation 0·1257 of a gramme of carbon, 0·0171 of a gramme of hydrogen, 0·0974 of a gramme of nitrogen, and 0·1114 of a gramme of oxygen. Now if we assume with Boussingault, that dry blood (after the deduction of the ash) contains 54·4% of carbon, 7·5% of hydrogen, 15·9% of nitrogen, and 22·2% of oxygen, and that the amount of nitrogen exhaled by the lungs is equal to half of that which is contained in the excrements, it follows that the bird experiences a daily loss of 0·1455 of a gramme of nitrogen, which is equivalent to 0·915 of a gramme of dry blood. In this 0·915 of a gramme of blood there is, however, only 0·498 of a gramme of carbon; and since the bird discharged 2·532 grammes of carbon daily in carbonic acid and the excrements, it obviously follows, that 2·034 grammes of the consumed carbon must have been yielded by fat.

No experiments on the subject of inanition are so worthy of notice as those of Chossat,* whose careful observations were continued for years, and embraced mammals, birds, and amphibia. In twenty-four cases, in which Chossat caused turtle-doves to die from starvation, the greatest daily loss of weight was manifested on twenty-two occasions at about the middle of the experiment, and twice on the day in which death occurred (excluding in this calculation the first day in which food was withheld, as some nutrient matter might then be taken up by the body from the contents of the intestinal canal). For some hours before death the body underwent no additional loss of weight. Taking the entire loss of weight which the animals suffered from the commencement of the experiment to their death as 1, it appeared that during the

* Recherches expérimentales sur l'inanition. Paris, 1843.

first third the loss was 0·393, during the second third it was nearly 0·260, and during the last third 0·347.

The entire loss of weight which the starving animal undergoes previously to its death varies very considerably with the species; thus Chossat found that rabbits (taking the mean of five experiments) died when they had lost 37·4% of their weight; guinea-pigs (five experiments) when they had lost 33·0%; turtle-doves (fifteen experiments) when they had lost 37·9%; domestic pigeons (twenty experiments) when they had lost 41·6%; hens (two experiments) when they had lost 52·7%; and crows (one experiment only being made) when they had lost 31·1%. As an average of all the forty-eight experiments 39·7% seems to be about the loss of weight which the body undergoes previously to death by starvation. Hence in the higher animals the organism loses from 1-3rd to 2-5ths of its weight before it succumbs to starvation.

Taking the averages in Chossat's experiments, it was found that the mammals, during the process of starvation, lost daily 4·0% of their weight, and the birds 4·4%, the mean of all the observations on both classes being 4·2%. We find, therefore, that the animal body loses daily about 1-24th of its mass by the metamorphosis of its tissues; a result which is in the most complete accordance with the result which had been already obtained by a different method (see p. 425), namely, that the daily quantity of properly selected food which an animal requires must amount to at least 1-23rd of its bodily weight.

Chossat has ascertained and compared in pigeons the relative losses of weight which each individual organ undergoes in cases of starvation—an investigation of the highest importance in relation to general physiology. We must here confine ourselves to the mere enumeration of the following results: the greatest amount of loss was experienced by the fat, 93·3% of this substance disappearing during the process of starvation; the blood suffered next in proportion, its loss amounting to 75·0%; of the muscles there disappeared 42·3%; of the bones only 16·7%; and of the nerves the least of all, namely 1·9%. If we compare, as Chossat has done, the total loss of bodily weight with the absolute amount of loss of the individual organs or tissues, it follows that the daily diminution of bodily weight may be thus sub-divided: half may be referred to the muscular tissue, a quarter to the fat, and the remaining quarter to all the other organs. Hence it is chiefly the products of decomposition of the muscular tissue and of the fat which are represented in the excretions.

Two very carefully conducted series of observations on inanition have been made by Bidder and Schmidt on cats. In one case the animal only sometimes obtained a little water; in the other case water was artificially injected into the stomach. The first series of experiments was made upon a cat weighing 2,572 grammes, which had been previously employed in a series of experiments on nutrition. The animal died on the eighteenth day of starvation; the loss of weight was tolerably constant from the third day to the period of its death; on the whole it lost 1330·8 grammes or 51·7% of its weight, the average daily loss consequently being 73·9 grammes or 2·87%; these numbers, as we perceive, far exceed those found by Chossat. During the whole duration of the experiment, the loss of weight was tolerably steady; from the first to the eighth day it corresponded to the quantity of carbon that was expired (0·56% to 0·58% of the weight of the body); subsequently the amount of carbonic acid which was excreted sunk less than the bodily weight: it was only during the two last days that the excreted carbon sunk very considerably as compared with the loss of bodily weight.

The secretion of urine at first diminished in a far more rapid proportion than the bodily weight, but afterwards, till the sixteenth day, the loss proceeded in each in almost the same proportion; the urine, like the carbonic acid, diminished considerably during the two last days. The urine was richer than usual in phosphoric and sulphuric acids; the chlorides disappeared after the first few days. The ratio between the sulphuric and phosphoric acids in the urine remained constant during the whole period of inanition.

From the tenth day of inanition all the bile that was secreted passed into the fæces. (Schmidt had calculated the quantity of bile which this animal should secrete from observations on cats in which biliary fistulæ had been formed; see vol. ii, p. 78.) The ingestion of water was found at every period of inanition to increase the urinary secretion and all its constituents, but it did not affect the exhalation of carbonic acid gas; hence we must conclude, with Schmidt, that the augmentation of the urinary secretion does not in any way depend upon a greater intensity of the process of inanition, but that it is solely dependent upon the circumstance that the urinary constituents, accumulated in the blood, are more rapidly eliminated by the agency of the water.

Since the muscular substance (with the connective tissue), when freed from fat, contains, according to Schmidt's analysis, 50·0% of carbon, 6·57% of hydrogen, 15·07% of nitrogen, 21·43%

of oxygen, 1·06% of sulphur, and 5·86% of mineral substances, we may calculate the amount of muscular tissue which is destroyed during the process of inanition by the amount of nitrogen contained in the excretions. Since during the whole process of inanition 30·807 grammes of nitrogen are given off externally, it follows that 200·43 grammes of muscular substance, free from water and fat, must have been consumed during these eighteen days. Since, further, 205·96 grammes of carbon were given off during the whole process, while only 102·24 grammes of this substance were contained in the 200·43 grammes of muscle, the remaining portion of the excreted carbon, amounting to 103·72 grammes, must arise from the oxidation of the fat. As fat contains on an average 78·132% of carbon, 132·76 grammes of this substance must have been oxidised. The animal has therefore lost, during the eighteen days' starvation, 200·43 grammes of muscle, and 132·75 grammes of fat; but the whole loss of weight being, as has been already mentioned, 1264·8 grammes, it follows that, with this loss of muscle and fat, there must have been a separation of 927·62 grammes of water. This amount of water is more considerable than it would have been if it had been merely the water pertaining to the lost muscular tissue which had been excreted; according to Schmidt, only 204·43 grammes of water pertain to that quantity of muscle; hence 653·5 grammes were abstracted from the remaining organs, which, moreover, on dissection, exhibited the appearance of being very poor in water.

Moreover, according to Schmidt's calculation, 76·5 parts of carbon are, on an average, given off for every 100 parts of oxygen that are absorbed during inanition. Of every 100 parts of water that were separated, 41·72 parts were given off in the perspiration, and 58·28 parts by the urine and fæces. With every 100 parts of carbonic acid, there were 75·15 grammes of water perspired. Schmidt has, moreover, determined the loss of weight of the muscle and fat for each individual day, from the amount of the excretions, in the same manner as we have calculated the loss which those tissues undergo during the whole process of inanition. It follows from these calculations that the quantity of muscular substance which undergoes decomposition sinks very considerably in the first two days (almost 50%), then to the ninth day it remains nearly stationary, from the ninth to the sixteenth day it again sinks very slightly, but on the two last days rapidly and very considerably. On the other hand, the quantity of the fat which is daily oxidised remains nearly the same from the beginning of the inanition to its

termination. On an average the loss of muscle which an animal experienced in 24 hours was 0·611% of its weight at the time, while the corresponding loss of fat was 0·422%; and they yielded 2·16% of carbonic acid, 1·6% of (perspired) aqueous vapour, 0·20% of urea, 0·008% of sulphuric acid, 0·011% of phosphoric acid, 0·029% of inorganic urinary constituents, 0·080% of dry fæces (in which was 0·02% of biliary residue), and 2·24% of fluid water separated with the urine and fæces.

In the second series of experiments Schmidt employed an adult cat, weighing 3047·8 grammes, into whose stomach 150 grammes of water were daily injected from the commencement of the process of inanition. The observations were only continued for one week, during which time the animal had lost 438·0 grammes in weight, and therefore 62·57 grammes daily. The daily excretion of nitrogen was 0·578, and that of carbon 4·740 for 1000 parts (by weight) of the animal; consequently, for 100 parts of the bodily substance 0·3835 of a part of muscle, and 0·3613 of fat were disintegrated, and together with 1·4670 parts of water were daily removed from the animal through the agency of 1·5749 parts of oxygen. It is obvious, from these numerical results, that the metamorphosis which occurs during inanition is considerably diminished by the abundant use of water; that is to say, that the body, during the process of starvation, experiences far less loss in albuminates and fat when water is freely allowed, than when (as was in part the case in the first set of experiments), there is a deprivation of this fluid.

Like Chossat, Bidder and Schmidt have attempted to determine the amount of loss of each individual organ during inanition. The body of the animal, which was employed in the first series of experiments, was used for this determination of the different weights. It appeared that, during the eighteen days' inanition, the blood experienced the greatest loss, namely, 93·7% of its original weight; next in order to the blood was the pancreas, which lost 85·4%; the loss of the adipose tissue with the mesentery was 80·7%; that of the muscles and tendons, 66·9%; that of the brain and spinal cord, 37·6; and of the bones, 14·3%: the loss experienced by the kidneys was the least, being only 6·2%. It is apparent from these determinations that the loss of weight in the body is mainly owing to the destruction of the muscular tissue, the blood, and the fat.

We must here mention certain experiments of J. Scherer's,*

* Verhandl. d. phys.-med. Ges. z. Würzburg. Bd. 3, S. 187-190.

which, although they only have reference to the urinary excretion, are of especial interest, as having been instituted in the human subject. He found that an adult man, for every kilogramme's weight of his body, discharged in twenty-four hours 29·5 grammes of urine, in which there were contained 28·4 grammes of water, 0·420 of a gramme of urea, 0·335 of a gramme of salts, and 0·346 of a gramme of extractive matters; while an insane patient (a man aged 50 years), who had resolved on starving himself to death, discharged, in a similar time, and for the same amount of weight, only 11·07 grammes of urine, in which were 0·176 of a gramme of urea, 0·167 of a gramme of salts, and 0·198 of a gramme of extractive matters. Hence the amount of urine in the starving man stands to that in the man living on an ordinary diet in the ratio of 1 : 2·6, while the solid constituents are as 1 : 2·4, the urea as 1 : 2·3, the salts as 1 : 5, and the extractive matters as 1 : 1·7. It is a very striking fact in these experiments, that at the very time when no nutrient matter is supplied to the organism, and when there is no excess of combustible materials for the process of oxidation, relatively more extractive matters were excreted than by the man living on his ordinary diet.

We now pass to the consideration of those relations of nutrition which are accompanied by an *increase of bodily weight.* This increase may possibly depend upon the typical augmentation of the individual organs within the limits of the highest development to which the organism can attain—consequently, upon *growth.* Although all the organs do not progress uniformly in this typical development, they yet simultaneously participate to a greater or less extent in this general increase and evolution,—the increase of one or other organ preponderating at the different periods of life. These are well-known facts, derived from anatomy and general physiology; but they draw our attention to the difficulties which oppose our endeavours to determine the metamorphosis of matter and the conditions of nutrition at this period of life.

An increase of bodily weight is, however, quite possible after the termination of growth; and daily experience shows us that this augmentation manifests itself more especially in two directions, namely, by a true *hypertrophy* of the most vitally active organs, as, for instance, the muscles, or by a more abundant deposition of adipose tissue in the panniculus adiposus of the skin, in the mesentery, &c.; but although this increase may be regarded as a normal condition of the human organism at a certain period of

life, it very frequently, however, assumes an abnormal or pathological character at this age. A similar remark refers equally to the fattening of agricultural stock,—a process which consists essentially in an augmentation of the fat in the organism, and very often assumes a course very different from that of normal nutrition; for we cannot regard the development of a fatty liver in geese, or the frequently observed partial disappearance of the nitrogenous constituents of organs, as, for instance, the muscles, in certain modes of fattening, as normal processes. Unfortunately, however, we are not entirely in possession of the conditions necessary to give any one special direction to the process of nutrition, by which we might be enabled to determine the relations already indicated. The difficulties which the unequal development of heterogeneous organs oppose to the determination of the metamorphosis of matter during the period of growth, depend upon the circumstance that we are not able to make nutrition assume any special form, either by means of food or any other external relations. The ingenious combinations of Liebig have sufficiently shown us the conditions under which, independently of proper food, a more abundant deposition of fat may be formed in the animal organism; and many of the investigations prosecuted by Boussingault and his pupils have confirmed this by the most striking proofs. Daily experience has further taught us that increased exercise of the organ gives rise to an increase of volume and weight exceeding the normal growth, whilst the deposition of fat is at all events very greatly favoured by the opposite relations. But although we have actually arrived at many general and clear ideas of these relations by means of laborious investigations and ingenious deductions, we cannot boast of being in possession of clear ideas based upon thoroughly exact inquiries. In accordance with the object of the present work, we abstain from all diffuse disquisitions and involved deductions, and limit ourselves to the facts yielded by exact inquiry.

Boussingault* has instituted some experiments on pigs, with a view of ascertaining the development of the *osseous system*, and with special reference to the mineral constituents.

I. A newly born pig weighed 650 grammes; its dried skeleton 48·25 grammes; the ash 20·73 grammes.

II. A pig aged 8 months weighed 60055·0 grammes; its dried skeleton 2901·0 grammes; the ash 1349·5 grammes.

* Ann. de Chim. et de Phys. 3me Sér. T. 16, p. 486-493.

III. A pig aged 11½ months weighed 67240·0 grammes; its dried skeleton 3407·0 grammes; the ash 1686·0 grammes.

The ash of these three skeletons, when burned perfectly white, contained:—

	I.	II.	III.
Phosphate of lime	84·1	91·3	92·4
Phosphate of magnesia	11·0	3·6	3·8
Carbonate of lime	4·5	3·6	3·4
Alkaline salts	0·4	1·5	0·4

According to this result, the pig aged 8 months, which was kept on ordinary food, gained on an average daily 11·7 grammes in the weight of the osseous system, 5·5 grammes of ash, 2·4 grammes of phosphoric acid, and 2·8 grammes of lime. The other pig, which lived 93 days longer, and was fed on potatoes only during that time, gained daily 6 grammes in the weight of the dry skeleton, 2·6 grammes of ash, about 1·4 grammes of phosphoric acid, and about 1·6 grammes of lime.

In the 544 kilogrammes of potatoes which the pig consumed during the last period of 93 days, there were 5440 grammes of mineral substances, including 615 grammes of phosphoric acid and 98 grammes of lime, whilst its skeleton had taken up during the same period of time 129 grammes of phosphoric acid and 150 grammes of lime. Consequently, 52 grammes more of lime were taken up than were contained in the potato ash. Besides this, there were 216 grammes of lime discharged with the excrements; consequently, 170 grammes of lime must have been supplied to the animal from some other source. Boussingault shows that this lime must be derived from the water in which the potatoes had been boiled.

We are entirely deficient in investigations instituted in a similar manner in relation to the development of other tissues or organs, when compared with the amount of food. But it would scarcely be out of place were we, before we enter upon the consideration of the increase in muscle and fat, to notice the experiments of Prevost and Morin, which connect themselves with the observations made by Baudrimont and St. Ange (see p. 369) on the respiration of the incubated egg. The results of these labours may be thus set down:—

100 parts of the contents of the *un-incubated* egg consist of—

10·72	parts of	fat.
16·53	„	matters free from fat, namely 8·19 in the albumen, and 83·6 in the yolk.
72·53	„	water.

After *seven days' incubation* 100 parts of the inner portion of the egg contained—

9·32	parts of	ether-extract.
13·94	„	dry matter, free from fat, of which 8·00 were albumen.
76·74	„	water.

The albumen itself	contained	34·9	per cent.	of dry matter,	free from fat.
The thick yolk	„	16·5	„	„	„
The liquid yolk	„	4·4	„	„	„
The membranes	„	2·0	„	„	„
The embryo	„	7·7	„	„	„
The liquor amnii	„	1·3	„	„	„

Consequently, during this period, the fat and the solid substances generally have diminished, while the water has been relatively augmented.

After *fourteen days' incubation* the inner membrane of the shell, the interior parts of the embryo, and, in one case, also the liquor amnii, exhibited an acid reaction. 100 parts of the inner portion of the egg contained—

9·46	parts of	ether-extract.
16·09	„	dry matter, free from fat, in which there were 7·7 parts of albumen.
74·43	„	water.

100 parts of	albumen contained	3·3	parts of dry matter,	free from fat.
„	the yolk	19·3	„	„
„	membranes	9·1	„	„
„	embryo	7·2	„	„
„	liquor amnii	1·4	„	„

After *twenty-one days' incubation*—

100 parts of	the interior of the egg contained	5·68 parts of fat.
„	„	15·44 parts of dry matter, free from fat, of which one-sixth consisted of yolk, one-sixth of yolk-membrane, and two-thirds of the embryo.
„	„	78·88 parts of water.

100 parts of	the yolk contained	29·0	parts of	dry substance.
„	membrane	20·6	„	„
„	embryo	14·6	„	„

The *weight of the egg-shell remained almost constantly the same.* The *fat in the egg* is of an uniform yellow colour before incubation, although it undergoes various alterations during the development of the embryo. On the seventh day a yellow oil was extracted by ether from the thick yolk, while the fluid yolk yielded first a yellow and subsequently a colourless fat. The membranes and the albumen yielded a transparent white oil, the liquor amnii a thick white fat, and the embryo a white fat like lard. On the fourteenth day the oil of the yolk became yellow and thick; the same was the case with the oil of the membranes; that of the albumen was colourless and thick; that of the embryo reddish and solid. On the twenty-first day the fat of the yolk became thick and of a pale yellow colour, and that of the membranes dark yellow and partially solid; ether extracted from the embryo a fat which at first was solid and yellow, but at a later stage was white and soft.

We will now simply subjoin the results of the *ash-determinations.*

Un-incubated eggs contained in—

	Dry substance, free from fat.	Ash.	Insoluble Phosphates.	Soluble Salts.
The White	15·090	0·85	0·13	0·68
The Yolk	15·166	0·90	0·90	0·00
	30·156	1·74	1·03	0·68

Eggs, after twenty-one days' incubation, contained in

The yolk	5·51	0·150	0·145	0 005
The yolk-membrane....	4·80	0·205	0·205	0·000
Putamen, chorion, and amnios....	0·42	0 040	0·015	0·025
The embryo	16·87	1·825	1·095	0·730
	27·30	2·220	1·460	0·760

According to Baudrimont and St. Ange, the absorbed oxygen is to the oxygen exhaled in the carbonic acid as 100 : 54·9 during the period of the development of the hen's egg from the 9th to the 12th day, and as 100 : 81·0 from the 16th to the 19th day,—a fact which is entirely in accordance with the circumstance that it is in the last third period of incubation that the greatest quantity of the

fat of the egg is consumed. The remaining results are readily obtained from the above numerical data.

Schmidt and Bidder have instituted a very admirable observation on a nearly full-grown cat, in reference to the assimilation of muscle and fat. This animal gained 337 grammes in weight in the course of eight days, when fed on flesh containing fat; the question therefore arose, whether the muscular substance only, or the fat, or both together, had contributed to this increase of weight. The animal had consumed during this experiment 1866·7 grammes of flesh, with 27·4 grammes of fatty tissue, and had eliminated 62·36 grammes of nitrogen. Now, since, according to Schmidt's analysis, the flesh consists of 70·26 $\frac{0}{0}$ of water, 5·71 $\frac{0}{0}$ of fat, 22·83 $\frac{0}{0}$ of muscular substance, and 1·2 $\frac{0}{0}$ of mineral matters, (the muscular substance, when free from water and salts, containing 53·01 $\frac{0}{0}$ of carbon and 16·11 $\frac{0}{0}$ of nitrogen), we may easily perceive that these 62·36 grammes of nitrogen must have been derived from the decomposition of 387·09 grammes of muscular substance, or of 1695·5 grammes of flesh. As 1866·7 grammes of flesh were consumed, the difference between the two quantities gives us 171·2 grammes as the quantity of flesh retained in the body. As, however, the increased weight of the body amounts to 337 grammes, the question arises, how far the remaining portion of the assimilated materials (155·8 grammes) is derived from assimilated fat or from the water retained in the body. These 387·09 grammes of decomposed dry muscular substance contain 205·20 grammes of carbon; but in addition to this nitrogen (62·36 grammes), 194·02 grammes of carbon were eliminated, and consequently 18·11 grammes remained in the body. Since, therefore, the muscular substance is more than sufficient to compensate for the carbon which has been excreted during the metamorphosis of matter, it is not conceivable that the fats, together with the muscular substance, can have participated largely in the oxidation; from hence Schmidt further concluded, and no doubt correctly, that the urea produced by the decomposition of the muscular substance must be separated through the kidneys before the remaining carbon and hydrogen of the muscular substance are exhaled in a state of oxidation through the lungs and skin. As only 1·98 grammes of fat are eliminated with the fæces in the form of saponified lime and magnesia, and as, according to Schmidt's analysis of the fatty tissue, 129·25 grammes of fat are taken up within the eight days, 127·27 grammes of fat are assimilated and remain in the body, in addition to the above

171·2 grammes of flesh and the 138·4 grammes of water. After the subjection of this calculation to the corrections required in consequence of various causes, and especially of the partial oxidation of the sulphur Schmidt reckoned that 40·16 grammes of muscular substance and connective tissue, 143·42 grammes of fat, 1·78 grammes of salts with sulphur, and 134·15 grammes of water, were assimilated in eight days by this animal, weighing 2177 grammes, and that in the case referred to the cat, for every kilogramme, daily assimilated 18·346 grammes of muscular substance and fat.

However indispensible such conclusions and the calculations based upon them may be for the purpose of obtaining a deeper insight into the metamorphosis of animal matter, we ought not to disguise the fact, that they only lead us to a very slight degree of relative certainty. Independently of the circumstance that slight deviations in the observation often lead to very different results, or justify very different conclusions, we must be conscious that in our inability to determine all these causes with exactness, or to represent them in an arithmetical form, we very often employ for our equations certain postulates, several of which may in the existing circumstances be equally probable, although they essentially modify our calculations. We must therefore here be cautious in dealing with illusive equations, which, although perfectly correct in an arithmetical point of view, may lead us into the most flagrant errors.

By feeding cats alternately with flesh and pure fat, Schmidt has moreover given probability to the view, that the albuminates are always more readily decomposed in the body than the fats, and that a diet consisting exclusively of fat (or of an insufficient amount of albuminates with an abundance of fat) causes the nitrogenous matters of the body to be subjected to metamorphosis, whilst the fats, which are taken up are, on the contrary, at first either entirely or for the most part deposited in the body, being oxidised at a later period, and probably only by degrees.

It is from this and a previously indicated point of view, that we must consider the results of those numerous experiments which have been instituted in reference to relations of nutrition during the fattening of animals generally, or of cows with a view of obtaining a more abundant supply of milk. In association with Schmidt's experiment, we have to notice an observation made by Persoz,* who fattened geese on maize; the blood of the geese

* Compt. rend. T. 18, pp. 245-254.

which had been thus fed was very rich in fat, but poor in albuminates; the quantity of the muscular substance diminished perceptibly, and where the fattening had been rapid the geese exhibited an absolute loss of bodily weight.

We do not here enter more fully into the individual series of experiments which have been instituted on animals in connexion with the process of feeding stock or of augmenting the quantity of milk; they were for the most part instituted solely in reference to what was formerly regarded as a very doubtful question (see pp. 211-216), whether food deficient in fat sufficed for the feeding or fattening of animals, and whether fat could be produced in the animal organism from the amylacea. They are consequently only of interest to us in relation to the latter point. Although Liebig at an early period demonstrated, partly by exact experiments, and partly by the most ingenious application of various facts which bore upon the point, that fat is formed in the animal body from carbo-hydrates, this proposition was yet for a long time denied by Dumas and Boussingault, and numerous experiments were made, some of which appeared to favour and others to oppose Liebig's view. As, however, we have already discussed this subject somewhat in detail (in vol. i., p. 254), we need here only mention two series of experiments, by which the correctness of Liebig's opinion was placed beyond all further question. Dumas,* in conjunction with Milne Edwards, repeated Gundelach's experiment of feeding bees with honey freed from wax (at all events the honey employed as their food only contained one-ten-thousandth part of wax). Of four swarms which were employed in the experiment, only a single one began to secrete wax and to build with it. The numerical results of this investigation may be most easily seen in the following manner:—

Fat which was found in the body of each bee at the beginning of the experiment	0·0018 of a gramme.
Wax which, on an average, each bee consumed with the honey during the whole of the experiment, did not exceed	0·0003 „
The whole amount of fatty matter whose origin might possibly be derived from the food, averaged for each bee at most	0·0022 „
During the whole length of the experiment the wax secreted by each bee averaged	0·0064 „
At the termination of the experiment the wax or ordinary fat in the body of each bee averaged	0·0042 „

* Journ. de Pharm. et de Chim. 3 Sér. T. 9, p. 339-344.

Finally, Boussingault* found by experiments on pigs that (to take an example) eight-months' pigs contained far more fat than had existed in their food, but that when they were fed solely on potatoes there was no more fat accumulated in them in the course of six months than corresponded to the amount of fat contained in the potatoes which they consumed; and that such kinds of food as potatoes, which could not of themselves be applied to the formation of fat within the body, acquired this property by a slight addition of fat or of albuminous matters.

In our previous notice of the quantitative metamorphosis of matter we have not done more than draw the balance between the ingesta and the egesta which we have observed in the living animal organism under various physiological conditions. It has been objected against this method, that it affords us no light whatever in reference to the interchange of the organic elements within the body in the process of nutrition; but independently of the fact that this is the only path we are able to pursue in order to obtain a general view, it has also led us to a number of facts which enable us to gain an insight into the intermediate stages of molecular motions in the body. It cannot, however, be denied that, notwithstanding many of the conclusions yielded by this method, we are still so ignorant of the *intermediate metamorphosis of matter*, that we can only adduce the facts known in reference to this subject, as mere appendages to our previous remarks. While we have endeavoured throughout the whole course of this work to notice all the important relations of each substance—substratum, fluid, and tissue—in reference to the metamorphosis of matter, we have always directed our fullest attention to this subject, which we regard as the crowning point of physiological chemistry, and the advance made in science during the last few years has indeed yielded the most extraordinary results in this respect. Notwithstanding many obvious deficiences and numerous imperfections, we see revealed before our eyes the image of a life rich in internal relations and external forms, and alike inexhaustible in the multiplicity of its phenomena and the incentives to future investigations. But still it is only a mere picture, in which many results of vegetative life are undoubtedly represented in too ideal a form; for whilst all phenomena are only parts of a motion regulated by definite laws, many portions of this sketch are drawn in false perspective. To find the correct perspective, we require to make a certain number of direct measurements,

* Compt. rend. T. 20, p. 1726.

since it will be impossible properly to introduce the different distances in the picture until the quantitative relations have been established and the points of sight mathematically determined. The present would seem a fitting place, in which to embrace the entire metamorphosis of matter in one grand comprehensive picture, which, being sketched in accordance with mathematical rules, may represent all the individual parts in their natural and real connection with one another. But unfortunately in physiological chemistry we are sadly deficient in these mathematical rules, by which alone we can ascertain the correct perspective of the individual parts of this picture of vegetative life.

There are very different methods by which we may obtain these geometrical points of sight; thus, for instance, in my investigations regarding the function of the liver and the formation of bile, I have adopted those points of sight which refer to the quantitative relations of the juices flowing to and from the liver; the results of these experiments, which certainly exceeded the very limited expectations I had formed of them, induced me in the case of other organs also to compare the ingesta with the egesta, and indeed far more important quantitative facts have already been obtained than one could have anticipated from the difficulty of procuring these egesta and ingesta in sufficient quantity, or in a condition adapted for examination, and from the very great deficiency of the means necessary for analysis. We have the more readily abstained from giving the fragmentary results of these yet unfinished labours, as they have already appeared in another place* with all the necessary details, and would seem to be better adapted to some of the earlier sections of this work.

C. Schmidt* has endeavoured to determine the intermediate metamorphosis of tissue in another way, namely by a net-work of mathematical lines; he simultaneously compared the constitution of the different transudations and of the blood, and attempted to establish the quantitative relations between the two, and to determine the laws which influence the elimination of matters from the blood through certain tissues into definite organs. We have incorporated the most essential conclusions of this work in our second volume; but notwithstanding many brilliant facts and conclusions, it soon became apparent that this method of investigation also failed in affording us correct answers to many questions.

In association with Bidder † Schmidt has tried a third method,

* Ber. der k. sächs. Ges. d. Wiss. zu Leipzig. 1853.

† Charakteristik der Cholera u. s. w.

by which probably the greatest advances have been made; it consists in the attempt to determine the amount of that motion which impels a very considerable fraction of the animal juices towards the intestinal canal. From the statements which have been previously made regarding the quantitative relations of the digestive fluids it appears, that according to Bidder and Schmidt's investigations and calculations, an adult man weighing about 64 kilogrammes [or 10 stone] secretes in twenty-four hours about 1600 grammes of saliva, in which are 15 grammes of solid matters, 1600 grammes of bile containing 80 grammes of solid matters, 6400 grammes of gastric juice with 192 grammes of solid matters, 200 grammes of pancreatic fluid with 20 grammes of solid constituents, and 200 grammes of intestinal juice with 3 grammes of non-volatile matters; consequently there are in twenty-four hours 10000 grammes of juices, containing 9690 grammes of water and 310 of solid substances, which pass from the blood into the intestinal canal, from which they are again for the most part resorbed. Since the body of a man weighing 64 kilogrammes contains about 20 kilogrammes [or 44 lbs.] of solid matters, and 44 kilogrammes [nearly 97 lbs.] of water, it follows that from 1-5th to 1-4th of the latter would be brought into the intestinal canal in the course of twenty-four hours, but only from 1-70th to 1-60th of the former. The coincidence between the amount of solid constituents in this collective sum of the digestive fluids and in the lymph (according to Marchand's determination), namely 3·1%, is a point of much interest. Since very careful analyses of the digestive fluids, as well as determinations of their amounts, were instituted by Schmidt, it is easy to see that we may obtain the most decisive conclusions from these numerically-established points, regarding the relative amount of this metamorphosis of matter within the body, as well in reference to the individual organic matters as to the elements in general. We may notice, as especially important in this point of view, the relations which have been established by these investigations between the biliary secretion and the respiration, and between the former and the urinary secretion. Thus, for instance, a dog for each kilogramme's weight consumes in twenty-four hours 8·6 grammes of carbon, while in the same time it excretes 1 gramme of biliary matter; 0·5 of a gramme of carbon of this biliary matter returns from the intestine into the blood hence it follows, that from 5% to 6% of the expired carbon has to go through the stage of bile-formation. This proportion is not essentially affected during a flesh-diet; but is altered by the use of highly amylaceous food, when the amount

of respired carbon considerably exceeds the quantity passing through the bile. When the mineral constituents of the food are much increased, the biliary secretion is relatively more increased than the respiration; but during starvation the former is more diminished than the latter. Of every 100 grammes of nitrogen which are separated by the kidneys, at most not more than 3 grammes pass through the bile (as taurine and glycine), while of 100 parts of sulphur from 54 to 86 parts take that course; under no conditions, however, does the whole of the sulphur pass through the stage of bile. In herbivorous animals scarcely 2-3rds of the glycine separated with the urine in the hippuric acid are contained in the glyco-cholic acid. During starvation we may put down the average typical relation as follows: for every 100 parts of expired carbon there are given off 15·4 parts of carbon, under the form of urea, by the kidneys. While in fasting animals (the calculations being made for equal bodily weight) the same daily quantities of carbonic acid and urea were secreted, the biliary secretion sunk to such an extent that on the tenth day of inanition only 2-5ths of the quantity of bile were obtained, which was secreted on the third day.

There are other interesting points of view which present themselves when we contrast, in relation to quantity, the elements of the intermediate metamorphoses of matter and those of the final excretions with the corresponding elements of the organism or of the blood; as for instance, when we compare the quantities of the carbon separated by the bile or by the saliva, with that which is separated by the kidneys or lungs, and reduce the numbers of both to 100 parts of the carbon contained in the organism or in the blood. As a standard of comparison Bidder and Schmidt employed results which they had obtained from a cat, and which, as they stand at present isolated to science, we must on no account omit. They found that each kilogramme's weight of the animal (which was a young cat weighing 1505 grammes) contained—

Muscles and tendons	450·36	grammes, or	when dry	107·64	grammes.
Bones	147·45	„	„	80·36	„
Skin	120·86	„	„	57·05	„
Intestinal tract	64·91	„	„	14·60	„
Brain and spinal cord	19·40	„	„	4·29	„
Liver	47·51	„	„	12·78	„
Lungs	10·78	„	„	2·24	„
Kidneys	9·00	„	„	1 85	„
Spleen	3·16	„	„	0·67	„

Pancreas	3·00 grammes, or when dry		0·66 grammes.	
Salivary glands	1·13	„ „	0·23	„
Heart	4·22	„ „	0·94	„
Aorta and Venæ cavæ	1·34	„ „	0·31	„
Mesentery, with its fat....	38·16	„ „	21·60	„
Eyes (including muscles and fat)	14·70	„ „	4·50	„
Larynx and trachea	2·28	„ „	0·75	„
Bladder	0·97	„ „	0·23	„
Testicles	0·41	„ „	0·09	„
Blood (which escaped during dissection)	60·36	„ „	9·60	„
	1000·00		320·39	

Hence in 100 parts of this animal there were contained 32·039 of solid materials. Schmidt employs these determinations in order to calculate the amount of the different elements, of the water, and of the salts in the body of the cat, and it follows from his calculations that in every kilogramme's weight of the cat there are contained about 679·61 grammes of water, 148·72 grammes of carbon, 20·19 grammes of hydrogen, 35·45 grammes of nitrogen, 54·78 grammes of oxygen, 2·43 grammes of sulphur, 1·88 grammes of sodium, 1·51 grammes of chlorine, 51·02 grammes of earthy phosphates, including about 0·4 of a gramme of iron, and 4·41 grammes of other salts, including 2·12 grammes of phosphoric acid.

This calculation gains additional support from the circumstance that, as follows from the data formerly given, a dog fed with flesh gives off 2·25 grammes of water by perspiration and respiration, and 5·97 grammes by the urine and fæces (and, therefore, on the whole 8·22 parts) for every 100 grammes of water which it contains, while 23·25 grammes are effused into the intestine with the intestinal juice. Hence the intermediate circulation of the water towards the intestine is far more considerable than its final excretion, and amounts to almost the fourth part of the whole quantity of water in the body. If, on the other hand, we compare the aqueous excretions with the amount of water in the blood, and fix the latter at 100, 27·9 parts are entirely removed from the body in twenty-four hours, while 79·0 parts are effused into the intestinal canal. Of every 100 parts of salts in a dog fed with flesh there are in twenty-four hours 5·3 parts given off to the external world, while 8·5 parts are effused with the digestive fluids over the surface of the intestinal canal; while of 100 parts of blood-salts 21·2 parts are completely excreted in twenty-four hours, and 34·1 parts conveyed into

the intestine. Of every 100 parts of carbon in the body 4·26 parts are separated by the respiration and urine, while only 1·31 parts pass into the intestine (of which 0·376 passes through the bile); and a similar ratio holds good with regard to the hydrogen. Of every 100 parts of nitrogen in the animal body, 3·89 parts are completely separated, and only 1·28 parts pass into the intestine (of which not more than 0·101 passes through the bile). Of every 100 parts of sulphur contained in the animal 3·3 parts are daily excreted by the kidneys, while 2·6 parts enter the intestine (1·7 of which passes through the bile.) Of 100 parts of phosphoric acid of the soluble phosphates of the animal body there are daily eliminated 7·27 parts, while 2·9 parts complete the circulation through the intestine.

These are only a few instances of results to which such statistico-chemical investigations of the intermediate metamorphosis of matter lead us, when they are conducted with that accuracy and circumspection which are indispensably requisite in such cases. As yet we unfortunately possess no other investigations of this nature than those of Bidder and Schmidt, of which we have made mention. But whatever ingenuity may be discernible in these inquiries, and however brilliant may be the results to which they have already led, it must be admitted that they have merely indicated the path by which more numerous investigations may enable us to reach the aim towards which we are striving. Since we are conscious of the deficiency of our knowledge, and the uncertainty of most of the facts in our possession, we likewise omit a mathematical, or rather arithmetical sketch of all the movements of matter in the living body considered in accordance with all their relations and value.

As it is our firm conviction, that it is only by the above indicated mathematical determination of the limits of the metamorphosis of matter that the general propositions of our science can be completely established, we are the more ready to leave to future chemists the bold attempt of classifying vital phenomena according to number, mass, and weight, and thus securing to their theories an amount of relative truth which might at all events equal that to which the other empirical sciences have long since attained.

In drawing towards the close of this work, we cannot forbear reverting once more to that department of our science, known as pathological chemistry; and the present would seem to be the fitting place for entering more minutely into the consideration of *pathological processes*; and this we had fully purposed doing, for our original intention was to investigate the pathological metamor-

phosis of matter after we had considered the same process in its normal character. Although we had occasion in almost every section on the juices and tissues to deplore our defective knowledge of their pathological relations, we yet endeavoured to collect all the scattered materials in our possession, and to combine them as far as possibe into one comprehensive whole, in order to obtain a basis for at least some few of the more tenable hypotheses and views; but it soon became obvious that it would have been necessary to deviate from the general plan of this work, if we had attempted to compensate for the absence of real facts by ideal combinations from amidst the confused mass of scanty, unconnected, and often careless observations. If we were not satisfied with mere speculations, we were driven to the necessity of ruminating once more over the observations and facts which had already been casually noticed in the course of this work; for we are deficient in the points of departure necessary to a scientific mode of treatment, while our explanations are wanting in certainty. Phænomenological data are indispensable to an ideal interpretation, although they can scarcely justify us in undertaking anything beyond a causal investigation. But can we be said to possess anything approaching a phænomenology of pathologico-chemical processes in the science known as pathological chemistry? Are we even in possession of investigations capable of exhibiting the causal connections of these pathologico-chemical phenomena? or are those which we do possess conducted with sufficient exactness to justify us in drawing from them any more general conclusions? What has been, or can as yet be done in pathological chemistry? Some few factors or resultants of the metamorphosis of animal matter have been investigated in a number of diseases, and in the most favourable cases the results have been compared together, although they very frequently did not admit of comparison. And even if the observations made on one and the same object in different conditions, did actually admit of comparison, we might indeed derive from them proofs or counter-proofs in reference to some popular view in humoral pathology, but they could never afford us any insight into the pathological process in the disease in question. It has only seldom been considered that it is indispensably necessary to the comprehension of a pathological process, that we should simultaneously investigate, if not all, at least many of the factors and resultants of one and the same object, and that we should endeavour to ascertain the mutual relations of the different parts of the group of phenomena. Instead of instituting accurate analyses of

the urine, the blood, the solid excrements, and the expired air in one and the same disease in one and the same individual, and making careful determinations of the quantities of the egesta when compared with the ingesta or the weight of the body, infinite pains have been taken to compare the composition of the blood in different diseases without a suspicion of the insufficiency of our analytical methods, and their inability to afford us any insight into the internal metamorphosis of matter. We believe that we have already sufficiently characterised the deplorable nature of most of the analyses of morbid urine. Diabetic urine has frequently been examined, the other juices have also been analysed in diabetes, and sugar has everywhere been found. Yet this much discussed disease has never been investigated with reference to the general metamorphosis of matter; on no occasion has any attempt been made to determine the ingesta and egesta of the body during its continuance; and even those experiments which have been made to determine the relation of nutrition to the formation of sugar, have either been left incomplete, or have utterly failed in their object, while the relations of respiration, which are so important in this disease, are still shrouded in complete obscurity. A comprehensive examination of the kind to which we refer is essentially needed in the case of inflammatory fever, or the inflammatory process accompanied by fever, which constitutes one of the main processes of most diseases. It would have served as the first point of attachment for a systematic inquiry, as the key-stone to a true system of pathological chemistry; a more favourable opportunity could scarcely be found for establishing and examining from a physical point of view these complicated relations in the deviations from the normal course of the metamorphosis of matter. But the ground before us is still unbroken, and the fruitful soil has as yet yielded little more than weeds.

In reverting once more to the points of view which afford a prospect of a successful elaboration of pathological chemistry, and in thus endeavouring to justify our silence in reference to pathologico-chemical processes, we in no way intend to animadvert upon those true inquirers who have exercised their powers on this uncultivated department; for the deficiencies in their labours were owing less to those who prosecuted them, than to the extraordinary difficulties of the pursuit, which will still require many years of labour to overcome: indeed, we have already endeavoured, throughout the whole course of this work, to place these difficulties in their true light, and to caution our readers against attaching too

high a value to the results yielded by this branch of science. We have often observed that pure chemistry, and more especially physiological chemistry, is still too incomplete to admit of the successful prosecution of such investigations, and hence the cause why so few chemists of celebrity have devoted themselves to pathological chemistry.

The cultivation of this department of science has therefore for the most part been left to beginners or mere chemical dilettanti, who too often were ignorant of even the first principles of physiology. It is to the anxiety of physicians to obtain chemical elucidations, to the imperfect training in the true method of physical inquiry manifested by these investigators, to their ignorance of scientific processes, and to their misconception of the true objects of pathological chemistry, that we owe those confused works which, instead of enriching pathological chemistry, have done nothing more than encumber and complicate it. In the hasty anxiety to turn all things to account, these carelessly and hurriedly collected materials have been indiscriminately applied to every possible diagnostic, prognostic, and other practical purpose. Such a method of proceeding, when carried to its extreme length, degenerates into mere purposeless uroscopy and other similar follies, which are not a whit better than the practices of the old water doctors. The labours of such medical handicraftsmen have at most only served to foster the flights of fancy of ready-writing journalists and ingenious physicians, who were not endowed with the mind requisite for earnest natural inquiry, and who, from the barren symbolization of sensuous perceptions and of confused hallucinations, have interwoven a complicated net-work of facts, which has been dignified with the title of humoral pathology.

Let us not, however, be discouraged by these drawbacks, which are inseparable from all newly developed sciences; but let us rather trustfully and hopefully look forward to a brighter future.

"THOUGH IT BE WINTER NOW, THE SPRING MUST COME AGAIN."*

* "*Es muss doch Frühling werden.*"

APPENDIX.

ADDITIONS* AND NOTES TO VOLUME I.

(1) Addition to p. 44, line 18.—We must not forget that oxalate of lime may possibly be formed during this process. We know that there is a close connexion between the excretion of uric acid and the formation of this salt, from the circumstance that in most specimens of urine, both sedimentary and non-sedimentary, oxalate of lime cannot be recognised by the microscope so long as the fluid is fresh, but as soon as crystals of uric acid present themselves, crystals of oxalate of lime (at all events in small numbers) may also be discovered; indeed, we generally find that in morbid urine the abundance of these crystals is proportional to the rapidity with which the free uric acid separates. Since uric acid, when acted upon by certain oxidising agents, may be decomposed into urea, allantoine, and oxalic acid, we may assume that a portion of the uric acid may be decomposed during this acid urinary fermentation, and that oxalic acid is formed from it,—a possibility which is converted into a probability by the recent observation of Ranke,† that uric acid, on the addition of yeast and of an alkali, becomes decomposed at a high temperature into urea and oxalic acid.

(2) Addition to p. 48, line 3.—Wöhler and Frerichs‡ have, however, shown by direct experiments that uric acid is decomposed in the animal organism in precisely the same way as by peroxide of lead, since they found that after the injection of urates there was not merely an augmentation of the urea in the urine, but also that oxalic acid was present in it in larger quantity.

(3) Addition to p. 50, line 19.—Scherer has likewise found formic acid, in association with other acids of this group, in the

* The "additions" are taken from the new German edition of this work published in 1853.

† Journ. f. pr. Ch. Bd. 56, S. 16.

‡ Ann. d. Ch. u. Pharm. Bd. 65, S. 340.

acid fluid of the spleen* and in leucæmic blood.† Further, very large quantities of this acid have been obtained, under my own inspection, from normal human sweat, the exact nature of the acid being not only determined by the reactions described in p. 50, but also by the determination of its saturating capacity and by elementary analysis.

(4) Addition to p. 56, line 8 from bottom.—Schottin believes that he has found metacetonic acid in the sweat; but considering the small quantities in which the acid in question occurs, and that formic, acetic, and butyric acids are also present, it must remain undecided whether this supposed metacetonic acid may not be merely a mixture of the two last-named acids.

(5) Addition to p. 61, line 5.—Schottin has determined the existence of butyric acid in the sweat with all the necessary accuracy, his investigations having been carried on under my own superintendence. Its quantity was, however, far less than that of the acetic and formic acids. It is, moreover, not a mere product of decomposition of the secretion of the sebaceous follicles, as I formerly believed, but occurs in a free state in the sweat of the axillary regions, the genitals, and the feet.

(6) Addition to p. 89, line 17.—Strecker‡ has discovered a body of much interest, which is isomeric with lactamide. He has termed it *alanine;* its formula is $C_6H_7NO_4$; and it is prepared in the following manner:—

If a mixture of 2 parts of aldehyde-ammonia and 1 part of anhydrous prussic acid be heated with an excess of aqueous hydrochloric acid, this substance is formed; it must be precipitated from the hydrochlorate of ammonia which is intermingled with it, partly by crystallisation, and partly by extraction with alcohol and ether; the hydrochloric-acid compound is decomposed by hydrated oxide of lead ($C_4H_4O_2 + C_2NH + 2\,HO = C_6H_7NO_4$).

Alanine crystallises in nacreous, oblique rhombic prisms, or in needles united in tufts; it dissolves in 4·6 parts of water at 17°, is slightly soluble in cold alcohol, but insoluble in ether; the aqueous solution has an intensely sweet taste, does not re-act on vegetable colours, and is precipitated by no re-agent. It sublimes

* Verhandl. d. phys.-med. Ges. in Würzb. Bd. 2, S. 298.

† Ibid. p. 321.

‡ Ann. d. Ch. u. Pharm. Bd. 75, S. 27-46.

at a temperature exceeding 200°, in delicate, snowy crystals. When rapidly heated it is partly decomposed; on being inflamed it burns with a violet flame. By the action of nitrous acid, alanine is decomposed into nitrogen, water, and *lactic acid.* The salts of alanine are crystallisable, and more soluble than alanine itself in water, as well as in alcohol and ether.

From this beautiful discovery of Strecker's it seems almost certain that lactic acid is formic acid coupled with aldehyde. If alanine consist of aldehyde and prussic acid, and if it is converted by nitrous acid into lactic acid, we need only assume that (as often occurs) the atoms of prussic acid are decomposed into formic acid and ammonia, and that the latter is decomposed by nitrous acid into nitrogen and water. Since, moreover, the products of decomposition of the lactates (at all events of lactate of copper), support the assumption that aldehyde pre-exists in lactic acid, this hypothesis regarding the composition of lactic acid must be regarded as well established.

(7) Note to p. 92, line 19.—[Scherer has recently published an excellent memoir "On the recognition of small quantities of lactic acid in animal matters," in the fourth volume of the Verhandlungen der physicalisch-medicinischen Gesellschaft zu Würzburg, 1854. After the coagulation of the albuminous matters, either by heat, or where this is not effectual, by alcohol, the filtered fluid is evaporated to dryness, any membranes that may be formed being removed. The residue is dissolved in water, and precipitated with baryta-water, in order to remove the phosphoric acid, sulphuric acid, and the earthy phosphates. The precipitate is removed by filtration; the excess of baryta is precipitated by sulphuric acid, and the fluid again filtered. The filtrate is treated with a little sulphuric acid, and is submitted to distillation, in order to separate the volatile acids; viz., acetic, formic, butyric, and hydrochloric acids. The residue left in the retort is very much concentrated, treated with strong alcohol, and allowed to stand for some days. The sulphates of potash and soda being insoluble in alcohol, crystallise and adhere to the walls of the vessel. The acid fluid is then decanted, and, after the addition of milk of lime, the alcohol is evaporated or distilled; we then filter while still warm, and remove the excess of insoluble hydrate of lime and the sulphate of lime that has been formed, and allow the filtered neutral solution to stand for some days. If the fluid should still exhibit an alkaline reaction from the presence of dissolved

hydrated lime in it, this may be removed by a current of carbonic acid gas through it and subsequent ebullition, when the lime will be thrown down as a bicarbonate.

If the quantity of lactic acid be not too small, and if there be not too much coloured extractive matter, the lactate of lime usually crystallises in a few days in wart-like clusters. If, however, these crystals do not appear, we evaporate the whole fluid to the consistence of a syrup, mix it with strong alcohol, and let it stand in a cylindrical vessel, which must be placed in a moderately warm situation. A resinous deposit, almost insoluble in cold alcohol, and consisting of a combination of lime with extractive matter, is generally soon formed. After the alcoholic solution has now become clear, we pour it into a vessel with a cover, and gradually add small quantities of ether. The lactate of lime, if present even in mere traces, separates in the form of delicate white threads and soft crystalline masses, which, after being dried upon filtering paper and re-crystallised from the smallest possible quantity of hot water, may be subjected to any further investigation that may be deemed necessary.—G. E. D.]

(8) Addition to p. 93, last line.—Although Schmidt long ago communicated to me that in his experiments he was unable to find any trace of lactic acid in the gastric juice of dogs, I have as yet been unable to determine the conditions under which it occurs in the gastric juice and those under which it is absent. Circumstances having prevented me from providing myself with a dog with a gastric fistula, for the purpose of repeating the experiments, I collected the gastric juice of fourteen dogs which had been condemned to death by the police; they had been fed with horse-flesh some (from 8 to 16) hours before they were destroyed, and a quarter of an hour before their death they were fed with fatty bones. The stomachs of most of the dogs contained no remains of the flesh, but merely fragments of bones. The most decided evidence of the presence of lactic acid in this gastric juice was obtained from the form and the characters of its salts, as well as from its saturating capacity. Since, moreover, the conditions, observed by Schmidt were also observed in this investigation, there could be the less doubt that in this case there was present not merely free hydrochloric acid, but also a considerable quantity of free lactic acid. On treating the gastric juice with lime-water, crystals, perfectly resembling those of lactate of lime, exhibited themselves on the evaporation, in vacuo, of the portion insoluble

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℞

168.88
48
120

in spirit: even if all the chloride of calcium were not extracted by alcohol, and if the transition of the acid to the magnesia, protoxide of iron, or oxide of zinc or of copper, did not allow us to recognise the acid, we might have concluded that these crystals were "hydrated chloride of calcium and lime," but the determination of the saturating capacity from the magnesian salt removed all doubt.

In accordance with my former investigations (see vol. ii, p. 44), I also found less hydrochloric acid than Schmidt, namely, only 0·118%, while Schmidt, never found less than 0·171% even in gastric juice which was mixed with saliva; in addition to the hydrochloric acid there was, however, also 0·391% of free lactic acid present (11·682 grammes of gastric juice saturating 0·072 of a gramme of baryta).

There can be no doubt, when we consider Schmidt's well-known accuracy as a chemist, that in the cases which he analysed the gastric juice contained no lactic acid, and that it was replaced by free hydrochloric acid. Amongst other points, Schmidt determined the amount of chlorine in the fresh gastric juice by strong acidulation with nitric acid and by precipitation with nitrate of silver; the precipitate was free from organic matter; after the excess of silver had been removed by hydrochloric acid from the solution (which had been freed from the chloride of silver by filtration), it was evaporated to dryness, incinerated and the bases combined with chlorine were analysed: the amount of these bases which was found was not sufficient to saturate all the hydrochloric acid calculated from the chloride of silver that was found. If now the free acid of a quantity of the same gastric juice were saturated with a solution of caustic potash or with lime- or baryta-water, it follows that exactly so much potash, lime, or baryta was required for saturation, as had been previously calculated for the excess of hydrochloric acid above the bases in the chloride of silver; this could not have been the case if alkaline lactates had been associated with the alkaline chlorides in the gastric juice.

(9) Addition to p. 98, 6 lines from bottom.—I have likewise detected lactic acid with certainty in the juice of the smooth muscles;* and Scherer has recently detected its presence in the juice of the spleen† and in leucæmic blood.‡ In our investigations

* Walther, Diss. inaug. med. Lips. 1851.

† Verhand. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 299.

‡ Ibid. Vol. 2, p. 324.

on the sweat both Schottin and myself failed in detecting it either in the healthy or morbid fluid. Robin and Verdeil * have recently found lactate of lime in large quantity in the urine of the horse, and Lassaigne† believes that he has found lactate of soda in the allantoïc fluid of a calf.

(10) Addition to p. 116, line 22.—[Damaluric and damoleic acids must be added to the oily fatty acids mentioned in the text. They were discovered by Städeler.—G. E. D.]

Damaluric acid ($C_{14}H_{11}O_3.HO$) was found together with damoleic acid amongst the products of distillation of cows' urine treated with hydrochloric acid; it is an oily fluid with a peculiar odour, not unlike that of valerianic acid, is somewhat heavier than water, in which it is slightly soluble, reddened litmus powerfully, and yields a white precipitate with basic acetate of lead, which under the microscope appears crystalline. Its silver-salt is not affected by light; its baryta-salt is crystallisable, soluble in water, renders turmeric paper brown, does not fuse when heated, and leaves, after smouldering, carbonate of baryta in the form of the original salt.

Damoleic acid ($C_{26}H_{23}O_3$) occurs with damaluric acid amongst the volatile acids of cows' urine;‡ it is fluid, heavier than water, in which it is only slightly soluble, reddens litmus, and forms a crystallisable salt with baryta, which, however, fuses on the application of heat.

(11) Addition to p. 124, line 10.—F. Kunde§ ascertained while working in my laboratory, that oleic acid, and likewise certain ethereal oils possess the property of producing the same colour with concentrated sulphuric acid and a little sugar as cholic acid and its conjugated compounds; and Schultze || has independently arrived at the same result. I am not, however, inclined to believe from my own observations that there is much probability of any mistake arising from this circumstance, since olein and oleic acid when mixed with sulphuric acid and sugar only slowly gave rise to this coloration, the process being dependent on an absorption of

* Mém. de la Société de Biologie. T. 1, p. 25.

† Ann. de Chim. et de Phys. 1850. T. 17, p. 295.

‡ Nachr. d. Ges. d. Wiss. z. Göttingen. 1850, S. 233-243.

§ Dissert. inaug. Berol. 1850.

|| Ann. d. Ch. u. Pharm. Bd. 71, S. 266-277.

oxygen, and, therefore only taking place in thin layers, as for instance, on a watch-glass.

(12) Addition to p. 137, line 20.—I* have likewise found creatine in the smooth muscles—in those namely of the stomach of the pig; and Siegmund† has subsequently detected it in the muscular substance of a pregnant uterus.

Verdeil and Marcet ‡ have found both creatine and creatinine in the blood.

(13) Note on Tyrosine, p. 142.—[Tyrosine has been recently analysed by Hinterberger,§ under Liebig's superintendence: it consists of—

Carbon	....	18 atoms.	59·67
Hydrogen	....	11 „	6·08
Nitrogen	....	1 „	7·73
Oxygen	....	6 „	26·52
			100·00

If tyrosine be treated with boiling nitric acid it yields, according to Strecker|| a large quantity of oxalic acid; but when treated with cold nitric acid it not only yields oxalic acid, but also nitrate of nitro-tyrosine $C_{18} H_{11} N_3 O_{16}$; which when treated with oxide of silver and ammonia yields $3\,Ag\,O + 3HO + C_{36}\,H_{17}N_4O_{17}$.

In addition to the sources of tyrosine mentioned in the text (namely casein, albumen, and fibrin), it may be obtained from horn (Hinterberger), cochineal (Warren de la Rue¶), and from feathers, hair, the elytra of the cockchafer, globulin, and hæmatin (Leyer and Köller**) by treatment with dilute sulphuric or concentrated hydrochloric acid, as well as by putrefaction. According to Hinterberger, tyrosine is much more advantageously obtained from cows' horn than from albumen, casein, &c., and it is better to fuse the horn with caustic potash than to employ dilute sulphuric acid. According to Piria,†† the following is the best method of obtaining this body: 500 grammes of horn shavings must be

* Walther, Diss. inaug. med. Lips. 1851, p. 8.

† Verh. d. phys.-med. Ges. zu Würzburg. Bd. 3, S. 50.

‡ Journ. de Chim. et de Phys. 3 Sér. T. 20, p. 91-93.

§ Ann. d. Ch. u. Pharm. Bd. 71, S. 70-79.

|| Ibid. Vol. 72, p. 70-80.

¶ Ibid. Vol. 57, p. 127.

** Ibid. Vol. 83, p. 332-338.

†† Ibid. Vol. 82, p. 251.

gradually added to a mixture of 3 litres [5·3 pints] of water and 1300 grammes of sulphuric acid, which must be previously raised to the boiling point; and the whole must be kept boiling for forty-eight hours; after dilution with much water and neutralisation with milk of lime, we treat the filtrate with a little more milk of lime and allow it to boil for an hour or two in order to decolorise it; the fluid, after filtration, is then evaporated to $2\frac{1}{2}$ litres, a stream of carbonic acid being passed continuously through it during the process; on being again filtered and allowed to stand the tyrosine separates in crystals. Leyer and Köller employ the following method: they boil 1 part of protein-substance with 4 parts of sulphuric acid and 12 parts of water for forty hours; the brown fluid is rendered alkaline by milk of lime, and is again heated and filtered. Sufficient sulphuric acid is then added to nearly destroy the alkaline reaction; the tyrosine now crystallises in tolerable purity from the evaporated filtrate.

With regard to *testing* for tyrosine, when its quantity is not sufficient to enable us to recognise its presence from its properties, and by its analysis, Piria recommends the employment of the reaction of the salts of tyrosine-sulphuric acid with neutral perchloride of iron, when a dark violet colour is manifested. If we place a little tyrosine (a few millegrammes are sufficient) in a watch-glass, moisten it with 1 or 2 drops of sulphuric acid, dilute it after half-an-hour with water, saturate it when heated with carbonate of lime, and add perchloride of iron (without any free acid) to the filtered fluid, the presence of tyrosine is indicated by the appearance of a dark violet colour.—G. E. D.]

(14.) Addition to p. 163, line 24.—Scherer* has obtained much more correct results than Becquerel in the case of children and adults. He found that the urine of young children contained on an average 1·7% of urea, while he found only 1·25% in the 24 hours' urine of a young man aged 22 years. Determinations of this kind lead, however, to few conclusions; to obtain an insight into the general process, our determinations should have reference to definite intervals of time, and to definite weights. A boy aged $3\frac{1}{2}$ years discharged in 24 hours 12·98 grammes of urea; a girl aged 7 years, 18·29 grammes; a youth aged 22 years, 37·008 grammes, and a man aged 38 years, 29·824 grammes. If, however, we take the relative weights into consideration, it follows that for 1 kilogramme's weight of the child there was discharged 0·810 of a

* Verh. d. phys.-med. Ges. z. Würzburg. Bd. 3, S. 180-190.

gramme of urea, while for 1 kilogramme's weight of the adult, only 0·420 of a gramme (or little more than half the quantity) of urea was excreted.

[Subsequently to the publication of the first volume, Verdeil and Dollfus* have found urea in large quantities in the blood of oxen. Moleschott† believes that he has found oxalate of urea, together with other oxalates, in the muscular juice of frogs, whose livers had been some days previously extirpated. Grohé‡ has, however, subsequently examined the constituents of the muscular juice of frogs in the Giessen Laboratory, and has arrived at the following results; namely,—

1. That neither urea nor oxalic acid exists in this fluid; and

2. That the crystals supposed by Moleschott to consist of oxalate of urea, in reality are composed of creatine, creatinine, and nitrate of potash.—G. E. D.]

(15) Addition to p. 171, line 5.—Chevallier and Lassaigne§ have extracted a substance to which they have given the name *xanthocystine*, from the miliary tubercles in a dead body that had been buried for two months. It was insoluble in water and alcohol, but dissolved in ammonia and in the mineral acids; the ammoniacal solution deposited minute white granules on evaporation; hexagonal tablets separated from the acid solutions on evaporation; the substance did not fuse on heating, but puffed up, became yellow and black, and developed an odour of burned horn, and gave off alkaline vapours. The investigation of this substance was not carried any further.

(16) Addition to p. 171, line 17.—The following is the best method of preparing hypoxanthine. The fluid obtained by boiling the spleen with water is precipitated by baryta-water; the filtered fluid deposits baryta-salts on evaporation, and must be refiltered and the baryta precipitated by sulphuric acid; all these baryta-precipitates contain hypoxanthine mixed with the phosphate, carbonate, and sulphate of baryta. It is extracted from them by a dilute solution of potash, and is precipitated from this solution, together with uric acid, by hydrochloric or carbonic acid. The hypoxanthine may be obtained in a separate state by dissolving

* Ann. d. Ch. u. Pharm. Bd. 74, S. 214.

† Arch. f. physiol. Heilk. Bd. 11, S. 493.

‡ Ann. d. Ch. u. Pharm. Bd. 85, S.

§ Journ. de Chim. méd. 3 Sér. T. 7, p. 208.

the precipitate in potash, and throwing down the uric acid by hydrochlorate of ammonia.

This substance has been found by Gerhard* (one of Scherer's pupils) in the blood of the ox, and by Scherer† himself in larger quantity in the blood in leucæmia.

We must know more about the occurrence of hypoxanthine, and its chemical constitution must be further studied, before we can venture to form a judgment, or even to offer an opinion, regarding its physiological value.

[We may take this opportunity of mentioning that Scherer,‡ has also found another body in the fluid of the spleen, to which he has given the name of *lienine;* it is crystalline, and according to Scherer's analysis contains no sulphur, but consists of C 53·71, H 8·95, N 4·82, and O 32·52—G. E. D.]

(17) Note to p. 181, line 6.—[Strecker§ has recently succeeded in forming taurine artificially from isethionate of ammonia, $NH_4O. C_4H_5O. 2SO_3$, which $= C_4H_7NO_6S_2 + 2HO$, and therefore only differs from taurine by two equivalents of water. This salt fuses at 120° C without disengaging ammonia, and Scherer hoped that at a still higher temperature it would lose water. He first found that taurine might be heated to 240° C without decomposition or fusion; and he then heated isethionate of ammonia to 236° C, and kept it at this temperature till it had lost 11$\frac{0}{0}$ of weight. The mass was dissolved in water; on the addition of alcohol it was precipitated in crystals; this precipitate, dissolved in water, furnished by spontaneous evaporation large crystals exactly identical with the crystals of taurine obtained from bile. Like taurine, they bear exposure to 240° without fusing or acquiring colour; they evolve no ammonia with a solution of potash; they do not precipitate the salts of baryta when boiled with nitric or nitro-muriatic acid; when fused with potash and nitrate of potash, they evolve ammonia, and the mass contains sulphuric acid. All these properties being the same as those of taurine, and its mode of formation proving that its composition is similar, this product is identical with the taurine of the bile.—G. E. D.]

(18) Addition to p. 196, line 2 from bottom.—It has been already

* Verh. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 299.

† Ibid. p. 323.

‡ Ibid. p. 298.

§ Compt. rend. T. 39, p. 63.

mentioned (vol. i, p. 84) that both Wöhler and Ure discovered that benzoic acid was converted in the animal organism into hippuric acid, and eliminated as such with the urine. The subsequent observations of Erdmann and Marchand* having shown that cinnamic acid undergoes a similar metamorphosis, it became a point of interest to ascertain whether the other acids homologous to benzoic acid, namely, toluylic and cumic (or cuminic) acids, were also transformed into hippuric acid; but this is by no means the case, as is shown by the independent investigations of Hoffmann† and of Ranke.‡ Moreover, the acids which are homologous to it in their amount of carbon and hydrogen, as salicylic acid, anisic acid, and cumaric acid, pass, like those previously mentioned, in an unchanged state into the urine, as was shown by Ranke's experiments.

(19) Addition to p. 218, line 4.—Scherer§ has found uric acid in considerable quantity, as a normal constituent, in the juice of the spleen. [Mr. Henry Gray (see his Prize Essay "On the Structure and Use of the Spleen," London, 1854, p. 209), being anxious to confirm the observations of Scherer regarding the presence of uric acid and hypoxanthine in the spleen-pulp, worked in one experiment on the spleens of twenty-five oxen, but wholly failed in detecting either of these substances; nor was he more successful with human spleens.—G. E. D.]

(20) Addition to p. 235, line 10.—*Pneumic* (or *pulmonic*) acid probably belongs to this group of conjugated nitrogenous acids. This acid, of which as yet we know very little, was discovered by Verdeil|| in the tissue of the lungs. The minced pulmonary tissue is stirred with water and exposed to strong pressure; the decanted acid fluid is heated in order to coagulate the albumen, and is then filtered, neutralised with baryta-water, and evaporated to three-fourths of its volume. After the removal of albuminous and some other matters by sulphate of copper, and the excess of the copper by sulphide of barium, we evaporate the fluid till crystals of sulphate of soda are formed; we then add a little sulphuric acid,

* Journ. f. pr. Ch. Bd. 35, S. 307-309.

† Ann. d. Ch. u. Pharm. Bd. 74, S. 342.

‡ Journ. f. pr. Ch. Bd. 56, S. 3-6.

§ Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 299.

|| Compt. rend. T. 33, p. 604, and Traité de Chimie anatomique et physiologique. T. 2, p. 460.

and boil with alcohol. The acid gradually separates from the alcoholic solution on cooling. It crystallises in oblique rhombic prisms (*F.* P. 5, F. 3), is extremely glistening, and refracts light strongly, loses no water of crystallisation at 100°, but at a higher temperature decomposes. It dissolves readily in water, is insoluble in cold but dissolves in boiling alcohol, is insoluble in ether, forms crystallisable salts with bases, and contains not only carbon, hydrogen, and oxygen, but also nitrogen and sulphur.

(21) Addition to p. 249, line 13 from bottom.—Many organs have a special tendency to accumulate large quantities of fat, when in *pathological states;* hence it is especially necessary to determine the normal quantities of fat which these organs contain. We particularly refer to the *liver*, *spleen*, and *kidneys*. We do not refer to those special fat-cells surrounded by connective tissue, such as we find in the *Folliculus adiposus cutis et renum;* but we here find the fat specially accumulated in cells not very unlike the ordinary epithelial cells. On making a microscopic examination of the liver in its perfectly normal condition at a certain period after a meal, it is very rarely that we find the hepatic cells perfectly free from fat. In the spleen, which naturally contains so large a number of colourless cells, we always find fat both in the carnivora and herbivora. Frerichs* discovered fat in the perfectly normal kidneys of dogs and cats, and von Hessling† constantly found it in the kidneys of fishes; and, finally, Lang‡ has demonstrated its ordinary occurrence in the kidneys of cats by microscopical and chemical investigations. In normal human kidneys, Frerichs observed small quantities of fat, and Lang found that fat was as often present as absent. Lang found from 1·8% to 3·9% of fat in the dried substance of the kidneys in cats, but he was unable to detect the presence of this substance in the kidneys of an ox or of a calf. It appears, both from pathological observations as well as from these investigations of normal kidneys, that the fat principally occurs in the cortical substance, and that it exists in the form of minute drops, which are partly free and partly enclosed in the cells of the tubules.

I must not omit to mention an observation which I have repeatedly made. I have seen the "canaliculi contorti" of the

* Die Bright'sche Nierenkrankheit u. deren Behandlung. Braunschweig, 1851, S. 43.

† Histol. Beitr. z. Lehre v. d. Harnabsonderung. Jena. 1851, S. 52.

‡ De adipe in urina et renibus, diss. inaug. Dorpat, 1852, p. 48-64.

kidneys of three freshly-killed deer, and of several hares, filled with free fat-globules, and the epithelium similarly filled, while scarcely an isolated fat-globule could be seen in the true tubular substance or in the contents of the bladder of these animals. Since these animals were perfectly healthy, and had certainly taken no fatty food shortly before their death, these observations to a certain degree oppose Lang's view, according to which the amount of fat in the normal kidneys is dependent upon the use of fatty food. At all events the subject requires further investigation, notwithstanding Lang's careful observations. On a recent occasion I could find no fat in the kidneys of a deer: could those three animals have been in a special state of development?

[We may here notice the investigations of Professor Beale* in reference to the amount of fat in the human liver and kidney both in health and disease.

	Healthy Liver.			
	I.	100 parts of solid matter.	II.	100 parts of solid matter.
Water	68·58	....	72·05	....
Solid matter	31·42	....	27·95	....
Fatty matter	3·82	12·15	4·28	15·31
Extractive soluble in water and alcohol; Extractive soluble in water only, and albumen	10·07	32·04	10·40	37·20
Alkaline and earthy salts	1·50	4·77	1·19	4·20
Matter insoluble in water, alcohol, and ether	16·03	51·01	12·08	43·22

	Healthy Kidney.	
	I.	100 parts of solid matter.
Water	76·450	....
Solid matter	23 550	....
Fatty matter containing much cholesterin	·939	3·98
Extractive matter soluble in water	5·840	24·79
Fixed alkaline salts	1·010	4·28
Earthy salts	·396	1·68
Albumen, vessels, &c.	15·365	65·24

* British and Foreign Medico-Chirugical Review, Vol. 12, p. 226.

Beale gives the results of his analyses of one kidney in a state of fatty degeneration, of four diabetic kidneys, and of two diabetic livers.

Taking the amount of fat in 100 parts of the *solid matter*, it was found that one diabetic kidney contained five times the normal quantity of fat; another four times as much; a third nearly the same proportion; and the fourth contained three times as much as was found in the healthy kidney. The fatty kidney contained rather more than six times the quantity of fat (26·97%) obtained in the healthy specimen.

Of the two diabetic livers, one contained only 4·64, and the other 7·85% of fat; while in the two healthy livers the corresponding numbers were 12·15 and 15·81%.

It would thus appear that in diabetes the kidney, in its chemical composition, approaches to that of fatty degeneration, while the liver appears starved, and its secreting cells seem to manifest a tendency opposite to that of fatty degeneration.—G. E. D.]

(22) Addition to p. 271, 11 lines from the bottom.—These experiments of Bidder have, however, most distinctly proved, by the most careful determinations of the excreta in fasting animals, that the elements excreted by the lungs and kidneys cannot solely originate from nitrogenous tissues, but that the excess of carbon and hydrogen excreted by the lungs is entirely to be referred to the decomposition of the fat of the starving animal, especially since these determinations of the excreta exactly coincide with the loss of fat directly observed in the dead body of the animal. The daily diminution of the biliary secretion in fasting animals occurs in almost the same ratio as the loss of fat in the body (Schmidt).†

(23) Addition to p. 280, line 17.—Busch‡ has applied the term *Inosterin* to a non-saponifiable fatty matter, which crystallises in needles, fuses at a little above 100°, is soluble in cold and hot ether as well as in boiling alcohol, from which it evaporates in an amorphous shape. He discovered it in a uterine tumour; it probably also occurs in the adventitious products known as collonema and colloid.

(24) Addition to p. 286, last line.—The test proposed by Maumene§ not only gives precisely the same reaction with

* Ber. d. kön. sächs. Ges. d. Wiss zu Leipz. 1851. S 162

† Verdauungsäfte u. Stoffwechsel. Mitau, 1852, S. 386-398.

‡ Müller's Arch. 1851, S. 358.

§ Compt. rend. T. 30, pp. 314 et 447.

glucose and the other true sugars, but also with other carbohydrates; for on heating all such substances to 100°, after the application of chlorine or metallic chlorides, they are converted into glistening black masses; this happens not only with sugar, but with woody fibre, hemp, linen, cotton, paper, starch, &c. Hence it is easy to see that this method is open to many fallacies, from the accidental presence of shreds of paper, dust, &c. If, however, we had to deal with pure substances, we might certainly recognise very small quantities of sugar, if, in accordance with Maumene's directions, we moisten, with the fluid to be investigated and then heat to 100° a pure woollen tissue (merino) which had been previously saturated with a solution of chloride of tin ~~and~~ afterwards dried. A glistening black patch is formed at the spot that had been moistened.

(25) Addition to p. 287, 1 line from bottom.—Moreover, this method must be employed with considerable circumspection in order to yield accurate results: for if the fluid which is being examined contains other organic substances, which can either combine with the alkali of the test-fluid, or can decompose oxide of copper even to a slight degree, either the alcohol-extract of the fluid, or the sugar-and-potash-compound, must be first exhibited before the test can be applied. A second objection to this procedure is, that we cannot keep the test-fluid for any length of time, and that we, consequently, ought to prepare a fresh quantity for each determination of sugar. In the course of time the alkali exerts a modifying action on the tartaric acid, so as to give it the property of reducing the oxide of copper with the co-operation of heat, and, indeed, even in the cold. If we have boiled the freshly prepared solution with the greatest care, and have convinced ourselves that no suboxide is precipitated, we still find that after a week a little of the suboxide is separated on boiling, and after it has stood for a longer time, a similar decomposition ensues, even at an ordinary temperature. This method is, however, by no means to be rejected for this deficiency; but at the same time we must not overlook it.

(26) Addition to p. 289, line 19.—C. Schmidt* has subsequently shown that sugar is a normal constituent of the blood of oxen, dogs, cats, and men; and I† have since found (almost simul-

* Charakteristik der Cholera u. s. w. 1850, S. 161-168.

† Ber. d. Gesellsch. d. Wiss. zu Leipzig. 1850, Bd. 3, S. 139-141.

taneously with Cl. Bernard*) that the portal blood contains no sugar, or only traces of that substance, while the blood of the hepatic veins is very rich in sugar. Bernard has satisfied himself that the sugar in the vessels near the heart gradually diminishes, and that only very little can be found in the arterial blood.

(27) Addition to p. 289, line 3 from bottom.—I have recently found sugar in the urine of a man suffering from a very well-marked attack of arthritis.

Alvaro Reynoso† has recently believed that he has found sugar in the urine in various bodily conditions, especially in cases of epilepsy and hysteria; he further believes that sugar is constantly to be found in the urine after narcotism has been induced by the inhalation of ether, also in pulmonary affections, and after the employment of the so-called hyposthenic agents, as metallic salts, sulphate of quinine, narcotic drugs, &c.; Uhle, who has had opportunities of most carefully examining the urine in all these conditions (for the most part under my own direct superintendence), has never been able to confirm any one of Reynoso's observations.

Bernard‡ found sugar in considerable quantity in the urine of the fœtus of the cow between the fifth and seventh months, and in that of the sheep at two months.

The same observer also found sugar in the fluids of the amnios and allantois of the calf, lamb, and pig. In a seven months' fœtal calf, sugar was found in the urine; but it no longer existed in the above-mentioned fluids.

(28) Addition to p. 290, 14 lines from the bottom.—Bernard§ has subsequently taken up this subject much more fully, while the fact that sugar exists in the hepatic tissue has been thoroughly confirmed by Frerichs,‖ Baumert,¶ and myself. The amount of sugar in the liver is much more considerable in many mammals and birds than in reptiles, while in the liver of fishes there appears to be no sugar. At all events, Bernard found no trace of sugar in the liver either of the eel or of the skate. In many diseases the sugar disappears from the liver.

* Arch. gén. de Méd. T. 18, p. 303.
† Compt. rend. T. 33. p. 410-416, p. 521, and T. 34, p. 18.
‡ Ibid. Vol. 30, p. 317.
§ Ibid. Vol. 31, p. 572-574.
‖ Handwörterbuch d. Physiologie. Bd. 3, Abt. 1, S. 831.
¶ Journ. f. pr. Ch. Bd. 54, S. 357-363.

(29) Addition to 291, line 15.—In examining the body of a person who died from diabetes, Bernard only failed in detecting sugar in the following organs, viz., the brain and spinal cord, the pancreas and the spleen.

(30) Addition to p. 298, line 19.—Guillot and Leblanc* believe that they have discovered milk-sugar in the blood of milch-cows.

(31) Addition to p. 299, top of page. [We must here notice *inosite* and *paramylon*, and give a few additional details regarding *cellulose*.—G. E. D.]

INOSITE. $C_{12} H_{12} O_{12}$.

Properties.—This variety of sugar crystallises with four atoms of water in colourless clino-rectangular prisms (*F.* P. 6, F. 6), which effloresce on exposure to the air, and lose all their water of crystallisation at 100° or in vacuo: it has a sweet taste, dissolves readily in water, slightly in strong spirit, and is insoluble in alcohol and ether; it crystallises from a boiling spirituous solution on cooling in glistening tablets somewhat like cholesterin; at a temperature exceeding 210° it fuses into a clear fluid, and at a still higher temperature it undergoes decomposition in the same manner as sugar. It undergoes no change when evaporated with hydrochloric acid, or when boiled with caustic potash. It forms a blue solution with sulphate of copper and potash; but there is no separation of suboxide of copper either on prolonged standing or on boiling; it does not undergo the vinous fermentation with yeast, but in the presence of casein or flesh it enters into lactic and butyric fermentation.

Composition.—Scherer,† the discoverer of this substance, has found that in the anhydrous state it is perfectly isomeric with anhydrous grape-sugar.

Preparation.—If we treat the muscular juice of the heart of the ox in the same manner as in the preparation of creatine from muscles, and if we then separate, by means of sulphuric acid, the baryta from the mother-liquid decanted from the creatine, and remove the volatile acids by evaporation of the fluid from which the sulphate of baryta has been separated by filtration, this sugar, together with sulphate of potash, crystallises from the remaining acid fluid on the gradual addition of strong alcohol. The crystals of inosite may be readily picked out and separated from those of sulphate of potash after the mother-liquid has been removed by pressure, or the

* Compt. rend. T. 31, p. 585.

† Ann. d. Ch. u. Pharm. Bd. 73, S. 322.

separation may be readily effected by boiling water, in which inosite is more soluble than sulphate of potash. Inosite may also be obtained, according to Scherer, without previous distillation, if we do not use quite sufficient sulphuric acid to throw down the whole of the baryta. On now shaking the solution with ether, till the liberated acids are separated, the inosite appears in beautiful crystals on the gradual addition of alcohol.

Tests.—Scherer* has given a very characteristic reaction for inosite, by which it may be distinguished from any other kind of sugar or carbo-hydrate. If we evaporate a solution of inosite, or a mixture containing that substance, almost to dryness on platinum foil, treat the residue with a solution of ammonia and a little chloride of calcium, and then carefully evaporate to dryness, a vivid rose-red tint is evolved, which allows us to recognise even 1–50th of a grain of inosite.

Occurrence.—This body has hitherto been only found in the flesh of the heart; Socoloff† sought in vain for it in the fluid from other muscular structures.

PARAMYLON. $C_{12}H_{10}O_{10}$.

Properties.—This variety of starch presents itself as a glistening white granular matter which, when freshly precipitated is translucent, and has a gelatinous and very swollen appearance: it is insoluble in water and in dilute acids; it is not converted into sugar either by dilute sulphuric acid or by diastase; and it is only by prolonged boiling with fuming hydrochloric acid that it yields a sweet fermentable substance. When heated to 200° it is converted into a gummy substance which is soluble in water, but not in alcohol: at a higher temperature it fuses and burns with an odour resembling that of sugar. Paramylon is insoluble in ammonia, but dissolves in caustic potash, from which it may be again thrown down by acids. It is not coloured blue by iodine.

Composition.—This body was discovered and analysed by Gottlieb‡; and was found to be isomeric with common starch:

Carbon	12 atoms	.... 44·44
Hydrogen	10 „	.... 6·18
Oxygen	10 „	.... 49·38
		100·00

Preparation.—Paramylon was obtained by Gottlieb from the

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 112.

† Ann. d. Ch. u. Pharm. Bd. 81. S. 375.

‡ Ibid. Vol. 75, pp. 51-61.

bodies of an infusorium, *Euglena viridis.* These animalcules after being freed as much as possible from other infusoria, were first treated with ether and spirit, and then with a boiling mixture of spirit and hydrochloric acid in order to remove the colour; the residue was mixed with water and thrown upon a cotton filter which allowed the granules of paramylon to pass, but retained the investing membranes of the animals. The substance was purified by solution in potash-ley, and precipitation with hydrochloric acid.

CELLULOSE. $C_{12} H_{10} O_{10}$.

Properties.—In its purest state this substance forms a spongy mass insoluble in all neutral menstrua, but very slightly soluble in alkaline solutions; it is convertible into dextrin both by sulphuric acid and by diastase.

If cellulose be treated with a mixture of four parts of concentrated sulphuric acid and one part of water, it swells on trituration into a clear jelly which at first is stiff but gradually becomes quite fluid: on the addition of water or alcohol there is a deposition of white flakes which are insoluble in hot water, alcohol, and ether, but possess the remarkable property of being coloured blue by iodine like starch; they differ, however, essentially from starch in this respect, that the iodine may be washed out with water and the blue colour destroyed, which is not the case with starch. This product of the metamorphosis of cellulose has hence been named *amyloïd;* its composition has been found to correspond with the formula, $C_{48} H_{41} O_{41}$. This substance is readily soluble in sulphuric acid, from which it may be again precipitated unchanged by water: it dissolves in strong nitric acid, without any development of gas; but on boiling there is a formation of oxalic acid: it only dissolves with difficulty in hydrochloric acid, from which it is not precipitated by ammonia; moreover, ammonia does not dissolve it. It swells in a strong solution of potash, and dissolves on the addition of water, from which it may be again thrown down by acetic acid. By the prolonged action of alkalies, cellulose is converted into a substance to which iodine communicates a dark violet, or almost black colour. Rotten potatoes contain a ferment which dissolves and destroys the cellulose, but in no way affects the starch.

The formation of this substance, and its reaction towards iodine, have been employed for the recognition of cellulose.

If, for instance, vegetable tissues, consisting of cellulose, be moistened with sulphuric acid and tincture of iodine, they assume a beautiful blue colour, which, however, gradually disappears on the addition of water. Moreover, chloride of zinc converts cellu-

lose first into a matter which is coloured blue by iodine, then into sugar, and lastly into a humus-like substance.

Composition.—According to Mulder, the composition of this substance is represented by the formula $C_{24}H_{21}O_{21}$; but according to the more recent observations of Mitscherlich,* it is perfectly isomeric with starch.

Occurrence.—Allusion has already been made to its occurrence in certain of the lower animals. We can obtain cellulose in its purest form from the pith or young roots of the elder by treating them with various indifferent, as well as acid and alkaline solutions, in order to remove any adhering soluble matter. Swedish filtering paper is pure cellulose.

(32) Addition to p. 314, line 10.—The bilifulvin of Virchow must not be confounded with the bilifulvin of Berzelius; the former seems to be identical with the *hæmatoïdin* also discovered by Virchow. Virchow† found hæmatoïdin constantly present in the extravasated blood consequent on the bursting of a Graafian vesicle in menstruation or conception, and he often noticed it in old extravasations of blood in the brain, in obliterated veins, in hæmorrhagic infarctus of the spleen, in subcutaneous sugillations, and in abscesses in the extremities. It appears from Virchow's investigations, that these crystals are formed in from 17 to 20 days after the extravasation has occurred.

Hæmatoïdin occurs in an amorphous condition in granules, globules, and jagged masses, as well as in perfect crystals belonging to the monoclinic system. These crystals are oblique rhombic prisms, not unlike crystals of gypsum: they often, however, occur as nearly perfect rhombohedra (*F.* P.6, F.3); they are strongly refractive and transparent, of a yellowish red, red, or ruby-red colour; they are insoluble in water, alcohol, ether, acetic acid, dilute mineral acids and alkalies. I have on several occasions seen the smaller and lighter-coloured crystals dissolve in alcohol containing sulphuric acid or ammonia, and again precipitated by ammonia; this, however, is not always the case. Virchow has accurately studied the behaviour of this body with concentrated alkalies and mineral acids: these reagents, however, do not seem to act uniformly on all specimens of hæmatoïdin; on the addition of hydrated potash the pigment usually assumes a glowing red tint, the mass gradually separating and breaking up into red granules, which slowly dissolve; the substance

* Ber. d. Akad. d. Wiss. zu Berlin. 1850, S. 102-111.

† Arch. f. path. Anat. Bd. 1, S. 383-445.

is, however, not again precipitated by the neutralisation of the alkali. If we allow concentrated mineral acids (sulphuric acid for instance) to act on hæmatoïdin, the clear outlines of the crystals disappear, and the colour of the roundish fragments passes first into a brownish red, then into a green, a blue, and a purple tint, and finally merges into a muddy yellow. Iron may occasionally, but by no means invariably, be found in the acid fluid that is formed during the decomposition of hæmatoïdin.

Virchow* subsequently discovered peculiar reddish-yellow, elongated crystals, which were either acicular or arranged in zig-zag rows or bars in the bile of persons who had suffered from cancer of the liver or retention of the bile consequent on catarrh of the gall-bladder; these crystals ranged from 0·005 to 0·010‴ in length, while the breadth scarcely admitted of measurement (*F.* P. 6, F. 2 and 4). They dissolve readily in caustic potash, but are not again precipitated by the addition of acids. Acetic acid has no effect upon the crystals; concentrated sulphuric acid makes them assume a somewhat darker colour, and gradually destroys them; moderately dilute nitric acid exerts little action on them. Besides these zig-zag crystals, to which (as has been already mentioned) Virchow assigned the name of "bilifulvin," he sometimes also found crystals which were perfectly similar to those of hæmatoïdin both in form and colour. While Virchow has repeatedly pointed out the great similarity which exists between this bilifulvin and hæmatoïdin, Dr. Zenker† (of Dresden) has recently discovered that if these substances are not identical, there is at all events the closest relationship between them, since he has proved that the bilifulvin may be very readily converted into hæmatoïdin. For if we allow bile containing bilifulvin to stand for a long time (several weeks) in contact with ether, the zig-zag crystals of bilifulvin disappear, and in their place we have crystals of hæmatoïdin (some of which are of very considerable size), which in their form, colour, and *micro-chemical reactions* are precisely similar to the crystals of hæmatoïdin formed within the body. Funke‡ has arrived at the same result simultaneously with, but independently of, Zenker. He allowed some bile containing bilifulvin to dry; on again moistening it, he found that the zig-zag crystals were replaced by light red crystals of hæmatoïdin. By a series of careful investigations Zenker has

* Op. cit. pp. 427-431.

† In a private communication. The details are to be published in Henle's Zeitsch. f. rat. Med.

‡ In a private communication.

arrived at the conclusion that as hæmatoïdin is always formed when blood in a stagnating state occurs in the body, so this substance, bilifulvin, is produced wherever bile stagnates.

(33) Addition to p. 330, line 26.—Dana* has recommended a very good method of detecting the presence of sulphur in organic matters containing that substance in not very minute quantity. We make a mixture of carbonate of soda, starch, and the substance to be tested for sulphur, and heat it by the blow-pipe on a platinum support; we then place the fused mass in a watch-glass with a drop of water, and add a small crystal of the nitroprusside of sodium discovered by Playfair;† if sulphur be present, that is to say, if sulphide of sodium be formed, the fluid will assume a splendid purple colour; most commonly a red tint first appears, which, assuming a shade of blue, becomes purple, and finally passes into a very deep azure blue, but even this is not persistent, for the fluid at last entirely loses all its colour.

Since the termination of Mulder's investigations on the protein-substances, several other views regarding the *constitution* of complex organic bodies have been promulgated. We have to a certain extent given up the older theory of organic radicals (on which Mulder's view is based), and have turned our views towards the establishment of conjugated compounds, salt-like combinations, and the like. The unexpected discoveries of the resolution (or cleavage) into other substances of amygdalin (Liebig and Wöhler), asparagin, salicin, and populin (Piria), the discoveries of the ammonia-alkaloids (Wurtz), and their theoretical constitution (Hoffmann and Kolbe), and finally, the observation that many nitrogenous bodies, when decomposed in various ways, yield special volatile alkaloids (Anderson, Rochleder, Wertheim, and others) give a certain support to the view that the protein-substances may have a constitution analogous to that of these complex bodies, and that there may be contained in them several proximate constituents conjugated together, or combined in the manner of salts. Thus, for instance, Wurtz‡ obtained methylamine from casein by treating it with alkalies, and Rochleder§ by decomposing it with chlorine, and the latter chemist consequently regards methylamine as one of the proximate constituents of casein. This view seems to gain support from the remarkable circumstance that there is an albuminous substance in

* Chemical Gazette. 1851. p. 459.

† Philosophical Magazine. 3 Ser. Vol. 36, pp. 197-221, 271-284, and 348-360.

‡ Compt. rend. T. 30, p. 9.

§ Ann. d. Ch. u. Pharm. Bd. 73, S. 56.

the blood of carnivorous animals which crystallises in prisms, while the corresponding substance in the blood of guinea-pigs and rats crystallises in tetrahedra. This obviously points at combinations of an analogous kind, in which only one different constituent has entered, which, however, is the cause of the difference in the crystalline form of the otherwise perfectly analogous body. Thus, for instance, according to Rochleder's hypothesis, one of these bodies might contain methylamine and the other ethylamine, in combination with the same group of atoms. We are, however, still deficient in the data which are requisite for the further elaboration of such an hypothesis, partly because the protein-bodies have as yet been little investigated in relation to these views, and partly because their decompositions, in so far as they are yet known, do not enable us to arrive at any definite conclusions on these points.

(34.) Addition to p. 332, line 9.—Panum* has contributed many important facts to our knowledge of the albuminous bodies and of their various reactions, and he has done much to correct our views regarding the coagulation of albumen and of similar matters by heat. He has especially shown, by numerous and very careful experiments, the influence exerted by the presence of salts or small quantities of acids on the separation of the protein-bodies at high temperatures. He found, for instance, that as a general rule, the temperature at which precipitation takes place is low in proportion to the amount of salt that has been added, and that the quantity of acid which is requisite to produce a permanent precipitation at the same temperature, is inversely proportional to the quantity of salt that has been added to the solution of albumen. Panum thinks that he is justified, from these and similar experiments, in considering all our previous ideas of coagulation as "confused;" but this conclusion is most distinctly to be drawn from his experiments, namely, that we must very carefully distinguish precipitated albumen from coagulated albumen. It appears, from my observations, that alcohol acts in relation to the precipitation and coagulation of albuminous matters in the same manner as the salts in Panum's experiments. By the gradual addition of alcohol we can depress the coagulating point of the fluid step by step, till we arrive at a point where the albuminous substance is precipitated, although not coagulated; and then, if not soluble in water, it still dissolves in solutions of the neutral salts of the

* Arch. f. path. Anat. Bd. 4, S. 17.

alkalies. As to what actually takes place in coagulation in those cases in which albuminous substances, under the influence of a high temperature, lose many of their other properties simultaneously with their solubility, we are perfectly ignorant, and Panum's experiments have thrown no light on this point.

(35) Addition to p. 332, line 17 from bottom.—Panum has also made some very interesting experiments on this point (the effect of acids on albumen), from which it appears that albuminous matters undergo essential changes even by acetic and ordinary phosphoric acids, so that it is not improbable that these acids, acting catalytically, may decompose the albumen into two new bodies. It does not appear from Panum's experiments that these acids enter into a definite combination with the albumen. One of the bodies arising from the action of acetic or phosphoric acid, namely *acid albumen*, is distinguished from the original albumen by its insolubility in concentrated solutions of neutral salts of the alkalies, and by its solubility in water.

(36) Addition to p. 334, line 20.—On passing a current of *carbonic acid* through a solution of an albuminous body, as, for instance, through the serum of the blood, white of egg dissolved in water, or a solution of the crystalline lens, a greater or lesser portion of the albuminous matter is always separated.

Panum regards this substance as casein, but milk-casein possesses this property in only the slightest degree. Melsens has made this observation on the white of egg, and, on instituting a microscopic investigation in union with Gluge, observed membranous matters, and hence he gave to this substance the name of "tissu cellulaire artificiel." I have treated all the known protein-bodies with carbonic acid, but never found that the precipitate, when examined under the microscope, presented any peculiarity; it certainly never had the slightest resemblance to any organic substance or to connective tissue. Moreover, Harting* has been at the pains of exposing the error into which Gluge and Melsens have fallen.

(37) Addition to p. 335, last line.—*Products of the metamorphosis of albumen.* The idea has long been entertained that the best method of deducing a formula for the composition of the protein-bodies, is from the study of their products of decomposition, and this view has given rise to that series of splendid investigations which have emanated from the laboratories of Liebig and of

* Nederl. Lancet. Sept. 1851.

Mulder. The discovery of tyrosine by Liebig, and the decomposition of the protein-bodies by oxidising agents, as illustrated by the investigations of Guckelberger and Schlieper, may be quoted as amongst the results which have sprung from this idea. But none of these investigations have led us to the goal which we had in view, since, for the most part, they only made us acquainted with the more remote products of decomposition. Mulder, however, in his search after a radical, has established several proximate products of metamorphosis, although he was unsuccessful in the attainment of his proposed object. Scherer, who was one of the first to submit the different protein-bodies to careful elementary analysis, instituted further investigations regarding their qualitative analogies and differences, and always sought to trace the proximate forms of metamorphosis of the protein-bodies, both as they occur naturally in healthy or diseased organisms, in special organs, or in the blood, and as they are artificially formed by the action of the less powerful reagents. Although as yet we have attained to no certain conclusion, or indeed to any conclusion whatever, we believe that this is the only course which can lead us to clearer views. If the discovery of the crystallisability of one of these substances has afforded us the means of obtaining it in a purer state than formerly, the analyses which I have hitherto instituted of the substance of the different crystalline forms have yielded us no definite distinction; hence we can here only refer to those products of the metamorphosis of the protein-bodies which may be considered as proximate products of their decomposition. The first of these which requires notice is albumen-protein.

(38) Addition to p. 336, line 26.—*Paralbumen* is an albuminous substance discovered by Scherer,* who met with it on several occasions in the contents of ovarian cysts. It is precipitated from the watery solution by alcohol in granular flakes; these, however, again dissolve in water at 35° in the course of a few hours, and give the same reactions as the body in its previous state of solution. The aqueous solution is rendered only slightly turbid by boiling, but thick flakes are deposited if acetic acid be then added, although this acid is altogether devoid of action in the cold solution. Nitric acid induces a considerable precipitate in the ordinary solution, while hydrochloric acid, on the other hand, only gives rise to a slight turbidity even when added in large quantity. Ferrocyanide of potassium, chromic acid, bichloride of mercury,

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 214.

basic acetate of lead, and tannic acid, throw down abundant precipitates.

Metalbumen is the name applied by Scherer* to another substance which he found in a dropsical fluid. Like the preceding substance, it is also precipitable from its watery solution by alcohol, and is again soluble in water; it is, however, not precipitable by acetic acid or ferrocyanide of potassium; moreover, on boiling the solution after the addition of acetic acid, there is a mere turbidity and no precipitate.

Similar substances have also been found in the urine in morbid states, especially in Bright's disease, and have received various names.

Mialhe and Pressat † believe that they have succeeded in tracing albumen through certain successive metamorphoses; they do not, however, base their views on satisfactory chemico-experimental evidence. According to them, *normal physiological albumen* exists in the fluids in a molecular state, and hence, not being actually dissolved, is not amenable to the laws of endosmosis; it is, moreover, characterised by its coagulability by heat and by the insolubility of the precipitate produced by nitric acid in an excess of the acid. Its first stage of metamorphosis is represented by the *amorphous casein-like albumen* which is produced by the action of the gastric juice; this is endosmotic, but not assimilable, and is imperfectly precipitated by heat and nitric acid; the precipitate induced by the latter is soluble in an excess of the acid. They apply the term *albuminose* to the endosmotic and assimilable substance which is finally produced by the action of the gastric juice on the albumen. Mialhe‡ maintains (without any additional evidence) that the substance precipitable by alcohol but again soluble in water, which Verdeil and Dollfuss§ found in the normal blood of the ox and called albumen, is identical with this albuminose. Mialhe|| has, however, the merit, notwithstanding many errors, of being the first closely to study the changes which the albuminous matters undergo during gastric digestion.

The *acid albumen* of Panum which has been already mentioned in p. 476, appears, from his subsequent and more carefully conducted experiments, to be likewise a product of the metamor-

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, p. 278.

† Compt. rend. T. 33, p. 450.

‡ Ibid. Vol. 34, p. 745.

§ Ann. d. Ch. u. Pharm. Bd. 74, S. 218.

|| Journ. de Pharm. et de Chim. 3 Sér. T. 10, p. 161-167.

phosis or cleavage of the protein-body under the action of acids. This substance, which has also been examined, although less accurately, by Melsens, is formed not only from the albumen of the blood and of white of egg, but also from fibrin and other protein-bodies; thus, for instance, I have seen it obtained from the crystallisable protein-substances. According to Panum, the body precipitated by acetic acid from the albuminous solutions saturated with salt possesses the following properties: when freshly precipitated it forms white flakes, which again dissolve very freely in pure water; they soon, however, lose this solubility on being dried, and especially on being exposed to the air, and likewise on being heated in saline solutions; on the other hand, their solution in water free from salt is not rendered turbid by the application of heat. We must here notice the remarkable circumstance, that when a comparatively large quantity of salt is in solution with the substance, a comparatively slight heat is required for the separation of the latter, and, conversely, that when less salt is present, a higher temperature is requisite to effect the precipitation. This substance does not exhibit an altogether uniform behaviour towards alcohol or towards metallic salts. Panum's analyses of this body shew that neither the acid which is added, nor the salt, exists in it in a state of chemical combination. Sulphur and phosphorus occur in far less quantity than in the original albumen.

Laskowski* obtained from albumen, and likewise from fibrin and casein, on treating them with a dilute solution of potash and afterwards with acetic acid, a product which closely resembled these substances, except that it was soluble in alcohol.

(39) Addition to p. 340, 11 lines from bottom.—Becquerel has recently employed an optical apparatus for the quantitative determination of the albumen in animal fluids, having availed himself of the discovery made by Biot and Bouchardat, that a ray of polarised light is deflected by albumen in the same manner as by sugar. The plane of polarisation of the light is turned towards the left; according to Becquerel, the degree of this deviation is proportional to the quantity of albumen that is present: the rotary power is 37° 36′; each minute corresponds to 0·180 of a gramme, and each degree to 10·800 grammes. It would appear from certain counter-experiments made by Becquerel, that this method is very trustworthy.

* Ann. d. Ch. u. Pharm. Bd. 58, S. 160.

(40) Addition to p. 349, line 21.—During the last few years it has been repeatedly maintained, that fibrin does not coagulate in threads, but in lamellæ. We may readily convince ourselves of the accuracy of the description given in the text, if we will take the trouble to use in the experiment inflammatory blood, in which the red corpuscles sink rapidly and the fibrin coagulates slowly. Funke has shewn in his Atlas (P. 19, F. 2) the coagulation of the fibrin from a fresh drop of blood, according to E. H. Weber's method; but here, on the one hand, the red corpuscles disturb the accuracy of the observation, and, on the other hand, we might regard the coagulation of the fibrin as the separation of a laminated mass, which readily forms plaits or folds on which the fibrillated appearance depends. The off-shooting of individual threads from the molecular granules which first become apparent, the projection of these threads, and their gradual augmentation in various directions, can only be seen in blood with a buffy coat. I am, however, unable to decide whether, at the final separation of all the fibrin, these filaments subsequently increase in two dimensions, that is to say, both increase in thickness and become converted into lamellæ or solid masses; if we observe dried blood, after the addition of water, with the microscope (as, for instance, the thin section presented by a small spot of blood, such as is often presented to us in medico-legal investigations), we see that everything dissolves or disappears except the so-called lymph-corpuscles and the fibrin; under these circumstances, in consequence, doubtless, of the thinness of the section, the fibrin certainly appears in the form of pure lamellæ, in which only a few distinct duplicatures are visible.

(41) Addition to p. 358, line 9.—I* could not find a trace of fibrin in the blood of the hepatic veins of the horse, while the portal blood was always tolerably rich in that constituent. Funke,† in his examination of the blood of the splenic vein, only found a little fibrin in a few cases.

(42) Addition to p. 359, line 20.—*Syntonin* is the name I have proposed for the substance which Liebig,‡ who was the first to describe it accurately, has termed *muscle-fibrin.* The following are its leading *properties.* When moist, it forms on the filter a

* Ber. der Ges. d. Wiss. zu Leipzig. 1850, S. 136.

† Dissert. inaug. de sanguine venæ lienalis. Lips. 1850.

‡ Ann. d. Ch. u. Pharm. Bd. 73, S. 125-129.

coherent, somewhat elastic, snow-white mass, which may be detached from the filter in plates or membranes; by extension and careful teasing, these delicate plates may be made to assume a fibrous appearance under the microscope, not unlike that of the blood-fibrin. The substance, when still moist, dissolves very readily in lime-water as well as in dilute solutions of the alkalies; it coagulates from the solution in lime-water on boiling, in the same manner as albumen; it is precipitated both from this and from the alkaline solutions by concentrated solutions of the neutral salts of potash and soda; the mass swells in a moderately concentrated solution of carbonate of potash, becomes gelatinous and dimly transparent, but does not dissolve; it is only after very considerable dilution that even a portion of the substance undergoes solution. If to the alkaline solutions of this substance we add chloride of calcium or sulphate of magnesia, we obtain no precipitate, unless we boil the mixture; if, however, we have previously boiled the alkaline solution (which at most only induces a slight turbidity), the solutions of the above-mentioned salts then at once induce a flocculent precipitate. Nitric acid throws down a white flocculent precipitate from the alkaline solutions of syntonin; chromic acid, or acid chromate of potash and hydrochloric acid, throws down this substance in flakes both from alkaline and from acid solutions; pure hydrochloric acid, even when added to excess, only renders the alkaline fluid opalescent. I was unable to dissolve uncoagulated syntonin in nitre-water (consisting of 6 parts of $KO.NO_5$ to 100 parts of water), even after five days' digestion at 30°.

With regard to its *composition*, Strecker* has found in this substance 1·4% of ash (from hens' flesh), 54·46% of carbon (from beef) and 53·67% of carbon (from mutton), 7·27% of hydrogen, 15·84% of nitrogen (from beef) and 16·26% of nitrogen (from mutton), and from 1·02 to 1·21% of sulphur. This substance is therefore sufficiently distinct in its composition from blood-fibrin. My analyses of the smooth muscles of the stomach of the pig, and of the middle arterial coat of the ox, agree tolerably closely with the analyses of Strecker. Walther† found rather more sulphur, namely, 1·6%.

The *preparation* of this substance is best effected in the following manner. We take flesh as free as possible from fat, mince it finely, repeatedly stir it with water, and press it till the fluid which

* Ann. d. Ch. u. Pharm. Bd. 73, S. 127.

† Diss. inaug. de musculis laevibus. Lips. 1851.

comes off no longer has an acid reaction or becomes turbid on boiling. The mass of flesh, which has been thus washed out, is then stirred with water to which 1-1000th of hydrochloric acid has been added. The fibre-substance of the muscles dissolves very readily in this fluid. On the neutralisation of its acid, the filtered fluid at first only yields a turbid jelly, so that the whole fluid either vibrates like freshly solidified glue, or presents a viscid semi-liquid condition; the jelly gradually condenses, and there sink to the bottom white, partially translucent flakes, which must be most carefully washed.

With regard to the *tests* for this substance, we may observe, that notwithstanding its many points of resemblance to albumen and blood-fibrin, it differs from them so essentially in some of its properties, that an error of diagnosis in this direction is hardly probable. Its behaviour towards water containing hydrochloric acid (in which blood-fibrin does not dissolve, but only swells), and towards nitre-water and carbonate of potash will prevent it from being confounded with blood-fibrin; while its precipitability from alkaline solutions by the chlorides of potassium and sodium, or by other salts of the alkalies, sufficiently distinguishes it from ordinary albumen.

The *occurrence* of this body, as the most essential constituent of the fibrillæ of the transversely shaped muscles, was first recognized by Liebig. I have found it not only in the ordinary smooth (unstriped) muscles of the stomach, the intestinal canal, and the urinary bladder, but also in almost all the contractile tissues in which Kölliker has detected the so-called contractile fibre-cells, as for instance, in the middle arterial coat, and in the spleen.

We are unable to form any definite opinion regarding the *origin* of the syntonin from the albuminous matters of the food, or from the albumen or fibrin of the blood, until we possess more distinct knowledge respecting the chemistry of the protein-bodies.

The *uses* of this substance are sufficiently obvious from the parts in which it occurs; it is the main constituent, and the most essential substratum of all the contractile tissues. We are, however, as yet unable to decide as to the extent to which it is more capable of contributing to vital contractility than the other protein-bodies.

(43) Addition to p. 385, line 14 from bottom.—From a comparatively early epoch in animal chemistry attempts have been made to recognise casein in the blood; but none of them were dis-

tinctly successful. Recently, however, very careful investigations have been made by several different persons, as for instance, by Guillot and Leblanc,* Panum,† and Moleschott,‡ which demonstrate the existence of a substance in the serum which appears to be different from the ordinary albumen, and which they hold to be identical with casein. Whether this substance is to be regarded as perfectly identical with ordinary albumen (as Scherer and I hold), the difference in its properties depending only on certain admixtures or incidental relations, is a point that possibly may never be decided; this much, however, is certain, that although the presence of casein in the blood is *à priori* in the highest degree probable (in consequence of its occurrence in other fluids), yet the identity of this constituent of the blood with the casein of the milk is by no means definitely established. Such questions as these can, however, never be thoroughly decided until we are better acquainted generally with the chemical constitution of the protein-bodies.

Guillot and Leblanc have obtained their casein by the addition of a few drops of acetic acid to blood-serum after the removal of its albumen by heat; and they maintain that they found in the precipitate all the characters of casein; they do not, however, state what these properties are. Anything like a doubt as to whether the substance precipitated by acetic acid was casein or albumen, or some other special substance, seems never to have occurred to these investigators.

The quantity of this substance precipitable by acetic acid was, according to their observations, different in different animals, and varies with the sex, food, bodily conditions, &c. It was especially abundant in the blood shortly before delivery, and during the process of lactation, the actual maximum occurring soon after delivery. In many pathological conditions this substance entirely disappeared from the blood.

The substance precipitable by acetic acid occurs, according to Stas,§ in very large quantity in the serum from the blood of the umbilical cord and the placenta.

Panum considers that the precipitate mentioned in p. 333, which is obtained by the dilution of the blood, especially after the addition of a little acetic acid, and which Scherer regards as albumen poor in salts and free from an alkali, is casein; and he

* Compt. rend. T. 31, p. 585.

† Arch. f. pathol. Anat. Bd. 3, S. 251-272.

‡ Arch. f. physiol. Heilk. Bd. 11, S. 105-111.

§ Compt. rend. T. 31, p. 630.

terms it *serum-casein*. On drying, this substance first becomes transparent and viscid, then glistening, hard, and tough, assuming, as Panum strongly urges, a beautiful green colour. Scherer,* under whose direction Panum conducted his experiments, correctly remarks, that the differences between this substance and albumen depend more on the nature of the fluids in which they occur, on the weakened action of the salts, the great quantity of the water, and the extremely minute disintegration of the separated matter, than on an essential difference in the nature of this substance as compared with ordinary albumen, and that casein is precipitated from concentrated, as well as from dilute solutions, while this substance is only precipitated from very dilute solutions by acetic acid. Panum remarks as characteristic of this substance, that it is precipitated from its solutions by carbonic acid: this observation is quite correct, but it stands in direct opposition to the view, that this substance is identical with casein; for as far as my experience goes, the casein of milk is not precipitated by carbonic acid, although the globulin of the crystalline lens is almost entirely thrown down from its watery solution by carbonic acid. Moreover, this substance, which may also be recognised in small quantity in the white of egg, presents a much closer resemblance to globulin than to the ordinary casein of milk. Panum has also found more of this substance in the serum of woman's than in that of man's blood (0·3%); and it was especially abundant in the serum of women shortly after delivery (from 0·99 to 1·25%).

Although Panum's experiments were very carefully made, and have led to the discovery of many new facts, yet the far less numerous experiments of Moleschott, who treated the serum, after the removal of the albumen by salts and coagulation, with sulphate of magnesia and heat, seem to afford far stronger evidence in favour of the existence of casein in the blood. I will here repeat, that neither Scherer nor I have ever ventured to deny, that in all probability casein exists in the blood; but until its presence in that fluid is actually proved, we cannot recognise its existence there. The discussion on this point is, however, little more than a war of words, for how can we strictly identify a substance with casein when we do not know what casein actually is, or rather believe that it is a mixture of two or more substances?

M. S. Schultze† has found a matter coagulable in the cold by acetic acid in the interstitial juice of the middle coat of the arteries,

* Jahresber. d. ges. Med. 1851, S. 75.

† Ann. d. Ch. u. Pharm. Bd. 71, S. 217.

and Moleschott* in that of the connective tissue, and of the ligamentum nuchæ; and I have found the same substance in all contractile tissues, which contain contractile fibre-cells (smooth muscular fibres).

Stas† found a similar substance in the fluid of the allantois.

(44) Addition to p. 386, line 15.

The Crystalline Substance of the Blood.

Properties.—This substance is distinguished from all other protein-bodies by the readiness with which it crystallises; but this very property merely indicates that we have not here to deal with a matter which is perfectly identical for all classes of animals, however extraordinary may be the resemblance existing between its different modifications; the crystals of the blood occur principally in three forms, namely, in prisms, tetrahedra, and hexagonal tablets. The prismatic forms, whose true system of crystallisation has not been firmly established notwithstanding the attention which has been devoted to the subject, are peculiar to human blood and to the blood of most mammals and fishes; the tetrahedra are met with in some of the rodents, as for instance, in guinea-pigs, rats, and mice, while the hexagonal tablets have hitherto been found only in squirrels. These crystals contain water of crystallisation, but lose it with tolerable rapidity when exposed to the air; they do not, however, at once fall to powder, but only partially contract and become irregular, still retaining a tolerable amount of water, as they are extremely hygroscopic. They are devoid of smell and taste; they are always red in colour, appearing of a peach-blossom or purplish red tinge when seen under the microscope; they are of a light cinnabar red when in masses, and of a yellowish brown colour when dried and pulverised. The solubility in water of the different forms of crystals is very different: thus 1 part of the tetrahedric crystals dissolves in 600 parts of water, while 1 part of the prismatic crystals from the dog requires no more than 90 parts of water; the solubility of the hexagonal crystals is nearly equally removed from these two extremes. They do not readily dissolve in water containing spirit, and they are insoluble in spirit of 85%; they are insoluble in ether, which is only capable of extracting some of the fat which remains mechanically mixed with the crystals. The aqueous solutions exhibit a peach-blossom colour in the case of

* Physiol. d. Stoffwechsels. Erlangen, 1851, S. 366.

† Compt. rend. T. 31, p. 630.

the tetrahedric crystals, and a dark pomegranate-red colour in the case of the prismatic crystals; the solution of the tetrahedric crystals separates into a brownish *coagulum* when *heated* to 63°; that of the prismatic crystals when heated to 64° or 65°. Small quantities of spirit produce no alteration in the aqueous solution, but when a larger quantity is added, a flocculent precipitate is formed, which is again soluble in water; a very large quantity of spirit or absolute alcohol precipitates the substance in clots, which are insoluble in water. When a little spirit is added to the aqueous solution, the substance coagulates at a lower temperature than in the pure watery solution. Ether does not produce any turbidity in the aqueous solution.

Cold concentrated *nitric acid* renders the crystals dark and almost black. On being heated, however, they become yellow and dissolve with tolerable readiness into a yellow fluid. The aqueous solution of the crystals yields a light brownish flocculent precipitate, even when very much diluted.

Hydrochloric and *sulphuric acids* do not give rise to any precipitates from the watery solution of the tetrahedric crystals, although they precipitate the solution of the prismatic crystals; this difference depends, however, solely upon the different concentration of the solutions; for if the solution of the prismatic crystals be diluted, as for instance, by the addition of four times its volume of water, no precipitate will be formed either with hydrochloric or sulphuric acid; but if, on the other hand, from four to six times the volume of concentrated hydrochloric acid, or an equal volume of English sulphuric acid be added to a solution of the tetrahedric crystals, this substance will likewise be precipitated.

The crystallisable substance is easily soluble in *acetic acid*, which simply changes the colour of the red watery solution into a brownish-yellow. If we *neutralise* with ammonia the fluid which has been acidified with acetic acid, pale brownish flakes are separated. Like other protein-bodies, the crystalline substance may be precipitated from the acid solution by yellow as well as by red prussiate of potash. It has also the further property in common with them, of being precipitated by neutral alkaline salts from the acetic-acid solution, or by acetic acid from the solution which has been treated with such salts. This precipitate which is thus obtained, is soluble in water, and exhibits very different properties from the original crystalline substance, a point to which we shall revert at a future page.

The crystals are insoluble in a concentrated *solution of potash;*

they are, however, very readily dissolved by a dilute solution of potash as well as by *caustic ammonia*, when they exhibit a brownish-yellow colour; this substance is precipitated from the alkaline solution by acetic acid in the form of light brownish flakes, and this is the case even when the fluid exhibits only a faint alkaline reaction.

Chlorine gas decolorises the solutions almost instantaneously, and precipitates white flakes.

An aqueous solution of iodine merely changes the red colour of the fluid into a brownish-yellow.

The salts of the *alkalies* and the *alkaline earths* do not give rise to any precipitates.

Nitrate of silver, bichloride of mercury, perchloride of iron, protochloride of tin, and neutral and basic *acetate of lead,* do not yield the slightest reaction, and it is only when ammonia is added to the fluid, which has been treated with salts of lead, that a very voluminous and grumous precipitate is formed.

Nitrate of protoxide of mercury and *bichromate of potash* give rise to very considerable dirty-white precipitates. Millon's test-fluid yields the reaction peculiar to all the protein-bodies.

Sulphate of copper leaves the fluid at first perfectly unchanged, but when it has stood for some time, it deposits an abundant pale greenish precipitate.

A solution of pure crystals becomes gradually *decomposed* on exposure to the air, although less rapidly than solutions which are mixed with other organic constituents of the blood. The crystals appear also to undergo a change when *dried in vacuo*, at all events their solution no longer presents the same bright red colour. The crystals begin to decompose at a temperature of 160° or 170°; at a higher temperature they swell considerably, and develope vapours which smell like burnt horn, and become strongly phosphorescent on being kindled: the substance is moreover readily consumed, leaving merely a small quantity of ash.

Alcohol renders the crystals insoluble in water, but it does not materially affect their shape—a remark which applies most forcibly to the tetrahedric form; the only change which they undergo being that their surfaces no longer appear perfectly plane; they remain nearly the same when heated to 100°. The coagulated crystals observed by Reichert* in the uterus of a pregnant rabbit were no doubt similar in character to these, for it is only the tetrahedra which, when treated with alcohol, exhibit all the

* Müller's Arch. 1849.

remarkable properties which Reichert noticed in the crystals on which he made his observations. Thus, for instance, they swell in dilute acetic acid, so that their diameters are increased three or four-fold; but they recover their former volume when washed, or when the acid is neutralised. They must, therefore, be secondary crystals, formed from the coagulation of the originally soluble crystallised substance.

Composition. The discovery of a crystallisable protein-substance appeared at once to afford a new means for obtaining more secure points of support for the establishment of its true constitution; but hitherto the elementary analyses of this substance have not furnished the desired information,—on the one hand, because the results obtained were too nearly identical with those yielded by the other protein-bodies, and on the other hand, because no guarantee of the perfect purity of the substance could be obtained. We must defer to a future page the consideration of the reasons which lead us to reject the validity of the results of former elementary analyses, and we will here only observe, that the membranes of the coloured blood-corpuscles and the coloured blood-cells penetrate through all filters and follow the blood-crystals, so that only a tolerably pure, and not an absolutely pure crystalline substance, can be obtained. In the mean while, we may at least hope to obtain a somewhat more definite insight into the constitution of this substance through its products of decomposition than we can possibly hope to attain in the case of the other protein-bodies. We have already mentioned that the different forms of the crystals of certain kinds of blood clearly show that the substances we have here to consider are homologous bodies, whose comparative analyses promise to afford at least some information regarding the constitution of these mysterious substances.

I have hitherto only analysed this substance from the blood of guinea-pigs, and hence I cannot venture to found any conclusion on such analyses; both tetrahedric crystals and the prismatic (those of the dog) are very poor in ash-constituents: I found that both kinds contained about 1% of mineral substances, the principal part of which consisted of oxide of iron, which frequently amounted to 72% of the ash; about 21% of the ash was phosphoric acid, while there was, moreover, a little lime and potash. This substance contained much less sulphur than is found in any other protein-substance.

As these crystals are always coloured, the question here sug-

gests itself, whether a special pigment (whose product of metamorphosis might be the well-known hæmatin, see p. 299) is here merely added to the true crystalline substance, and either crystallises with this substance as an isomorphous body, or only colours it in the same manner as uric-acid crystals are commonly coloured by the colouring matter of the urine, or whether we are here considering only a single ferruginous, crystallisable substance, of which hæmatin constitutes one of the separated products. I have not yet been able decisively to determine this question, but several facts seem to me to afford the greater amount of probability to the latter of these views.

Products of its metamorphosis. These substances have not yet been analysed with any satisfactory amount of exactness; we will therefore simply observe, that this protein-substance, precisely in the same manner as albumen, after being treated with acetic acid and alkaline salts, yields a substance which is altogether analogous with Panum's *acid albumen.* The aqueous solution of this substance does not exhibit the slightest turbidity on boiling, but when a larger or smaller quantity of an alkaline salt is added to it, a precipitate will be formed at a lower or higher temperature, precisely the same as in the case of acid albumen. An excess of salt precipitates this substance, even at an ordinary temperature; hence we may obtain it entirely free from acid, after repeated solution in water and precipitation by salts. When the solution containing an acid is neutralised by potash or ammonia, a considerable deposite is formed, which dissolves in ammonia, but is precipitated from it at a gentle heat. Nitric and sulphuric acids throw down copious precipitates from the aqueous solution, but hydrochloric acid does not produce such an effect. Ferrocyanide of potassium occasions a considerable deposite without any special addition of acid. Sulphate of magnesia, alum, sulphate of copper, chloride of iron, protochloride of tin, and neutral acetate of lead do not produce any precipitates even by boiling, but precipitates are thrown down by basic acetate of lead, nitrate of silver, bichloride of mercury, and nitrate of protoxide of mercury.

I am still engaged in the analyses of this substance, as well as in the investigation of other products of decomposition of the crystalline substance.

Preparation. The crystals of the blood, which may certainly have been seen by many earlier investigators, but which were first

observed by O. Funke,* were prepared exclusively for microscopical examination by him and by F. Kunde,† to whom we owe the discovery of the tetrahedric and the hexagonal blood-crystals; the method they employed was, to cover a minute drop of blood with a glass slide, and after a small quantity of water, alcohol, or ether had been poured upon it, the whole was exposed to gradual evaporation. I have now succeeded,‡ by different methods, in exhibiting these crystals on a large scale and with tolerable quickness, and in all these modes of preparation light and atmospheric influences constitute the most essential conditions towards the rapid formation of these crystals. The method of preparation frequently requires to be very considerably modified in different kinds of blood. Funke has shewn, in his careful experiments on the mode of formation of these crystals under a glass slide, that it is essentially necessary that the blood-cells should first burst before crystallisation can begin, and the only available means are water, alcohol, and ether, as has been shown by Funke and Kunde. The evaporation which occurs after the formation of the crystals under a glass slide, is by no means so important as it would appear, since, for instance, the blood (of guinea-pigs) may be diluted with twice its volume of water, and yet the crystals may be perfectly separated in the course of three-quarters of an hour after the employment of a proper method of treatment; in other soluble crystals, as, for instance, in those of the dog, it is necessary to facilitate their separation by the addition of an adequate amount of alcohol.

Tests. Although this substance differs so essentially from all other protein-bodies by its capacity for crystallisation, its indifferent behaviour towards moderately diluted hydrochloric and sulphuric acids, towards nitrate of silver, neutral and basic acetate of lead, bichloride of mercury, &c., it is extremely difficult and sometimes even impossible to recognise it, when it is present only in small quantities, or when it is mixed with many other protein-substances. Since other protein-bodies or their immediate products of metamorphosis share at least in some of the properties which appertain to it, its presence in a mixture of protein-substances, could not be regarded as thoroughly proved, until its crystals had

* Dissert. inaug. Lips. 1851; and Zeitschr. f. rat. Med. N. F. Bd. 1, S. 814-192, Bd. 2, S. 199-244, u. 288-292.

† Zeitschr. f. rat. Med. N. F. Bd. 2, S. 271-287.

‡ Ber. d. k. sächs. Ges. d. Wiss. 1852, S. 23-26, u. 78-84.

been obtained. But is it not probable that all the protein-bodies, or a substance separated from mineral matters and common to all of them, may crystallise? But even when crystals have actually been obtained from an albuminous fluid, it requires a very careful investigation to prove their identity with the crystalline substance of the blood.

Physiological relations. We have already remarked in the preceding pages, that the crystallisable substance of the blood is limited to the coloured blood-corpuscles, as Funke has especially shown to be the case. It would appear, however, from experiments made on the subject, that it occurs in all red-blooded animals, although it may present the various modifications which have already been noticed; it is also more readily obtained from certain kinds of blood than from others.

We must yet enter somewhat more circumstantially into the mode of preparation of the crystallisable matter, since this subject is one of importance, when considered in reference to many still doubtful points referring to the blood. The blood-crystals are formed from blood containing fibrin and serum, as well as from blood which has been deprived of its fibrin, and possibly also from cruor freed from serum. Under certain relations, they are formed so rapidly and in such great quantities, that they frequently appear where one would the least expect to meet with them. Thus, for instance, they occur in great abundance whenever blood-clots (as, for instance, from men, cats, and dogs) which have only been roughly chopped, and which have been frequently although imperfectly washed in water, are suffered to remain for some time exposed in a moist state to the air, either in ordinary light, or, what is better, in sunlight; when thus treated, the superficial parts of the pieces of fibrin are rapidly covered with entire crusts of the most beautiful and large crystals. I obtained the tetrahedric crystals, to which I have already referred, most rapidly, that is to say, in 35 minutes after the animal had been killed, from the blood of guinea-pigs; the defibrinated blood, after being diluted with water and treated in the manner described in the preceding page (an aqueous extract of the cruor may also be employed for this purpose) is exposed for 15 minutes to a stream of oxygen either in broad day-light or sun-light, and carbonic acid is then conducted through the lighter red fluid for five, or at most ten minutes; the carbonic acid gradually renders the fluid darker, but it soon becomes more and more turbid; in accordance with the degree of its turbidity, the fluid exhibits a more or less bright vermilion red tint

from the separated crystals which, when the stream of carbonic acid is interrupted, gradually sink to the bottom, and form a considerable bright vermilion-coloured sediment. Much the same method must be employed to obtain the prismatic crystals from human blood or the blood of cats and dogs; but in this case it is necessary to have recourse to several other conditions, which will subsequently be noticed. These crystals may indeed be separated by rinsing from all the constituents of the serum and from the greater part of the colourless blood-corpuscles, as well as from the cell-membranes of the coloured corpuscles, but still, notwithstanding repeated rinsings, many of the latter frequently remain, in consequence of having served, to a certain extent, as points of deposite for the crystals which thus enclose them; and hence they are not adapted, when in this condition, for elementary analysis. They must therefore be dissolved in water, and carefully filtered, in order perfectly to free them from all morphological particles. The re-crystallisation, however, presents great difficulties. We will here merely observe, that we cannot employ a high degree of heat on account of the coagulability of the substance, or the air-pump on account of the amount of gas necessary for crystallisation. We may, moreover, recognise that the solution before us is that of a pure crystalline substance, from the fact that it cannot be precipitated by bichloride of mercury, nitrate of silver, or basic acetate of lead. The coagulum, which is obtained by heat from the crystalline solution, is at all events so far unsuited to elementary analysis, that it does not represent the pure crystalline substance; for during coagulation the crystalline substance loses not only carbonic acid and phosphates, but also about 1·2% of organic matter, which consists of a strongly re-acting acid and of a nitrogenous body, bearing some remote resemblance to glutin.

The numerous and variously modified experiments which I have instituted on this subject, lead me to regard light merely as an auxiliary in the crystallisation; for although crystals are certainly also formed in the dark, or even in the night under otherwise similar conditions, they are only gradually deposited, and always in far smaller quantities; thus, for instance, I could never obtain more than 2% of crystals from the blood of guinea-pigs in the dark, whilst I was frequently able to procure more than 7% of dry crystalline substance during ordinary daylight, or in sunlight. That which has been already stated in reference to light, applies very nearly with equal correctness to the application of oxygen. We may not unfrequently succeed, even without the

use of oxygen, and by the mere application of carbonic acid, in obtaining these crystals in sun-light; but then only in far smaller quantities than in those cases in which the blood had been previously impregnated with oxygen. I discovered, from a series of comprehensive quantitative determinations, the particulars of which I have elsewhere* given, that the crystals are formed with far the greatest rapidity when the oxygen is suffered to pass through the blood in a slow stream for about 15 minutes before the application of the carbonic acid; for if carbonic acid be first, and oxygen be subsequently passed through the blood, the latter appears to hinder the process of crystallisation; but when the fluid is introduced into carbonic acid after it has been impregnated with oxygen, the crystallisation begins almost instantaneously. This crystallising process appears, moreover, to occur with a rapidity proportional to the length of time that the fluid has been in contact with the oxygen before the application of the carbonic acid.

Different microscopical observations have appeared to show that the presence of fibrin is inimical to the formation of crystals, and that serum is indispensable to their production, but, as we have already observed, the presence of fibrin exerts no action, either favourable or the reverse, on the crystallisation. The serum is equally devoid of all influence on this process, for crystals, and some very pure ones, may even be obtained from the later rinsings of chopped blood-clots, after they have been stirred and washed three or four times with water, although they certainly cannot retain any great amount of serum. No crystals, bearing even a remote affinity to the above-described blood-crystals, can be obtained from the serum either by these means, or by microscopical treatment under glass plates; hence we are scarcely going too far when we assert that observers who, like Robin, assert that they have procured the true blood-crystals from the serum, are entirely mistaken, and that they would be perfectly correct in regarding such crystals, which were noticed by every careful observer long before the discovery of the true blood-crystals, as mineral salts.

Although I very reluctantly enter upon the discussion of a subject which is still being made the object of inquiry, and cannot therefore be determined pending such an examination, I have thought that I could scarcely any longer avoid giving some notice of it. The observations to which I have already referred, together

* Ber. d. königl. sächs. Ges. d. Wiss. zu Leipz. 1853.

with others, incline me to believe that this crystalline substance is not a mixture of a pigment and a protein-body, but a pure chemical compound; the difference in the form of the crystals of different kinds of blood seems to indicate with tolerable certainty that this compound must, however, be either a salt-like or a conjugated compound. All the analyses which I have hitherto made of the pure substance have failed, like all previous elementary analyses of the protein-bodies, in yielding any definite views as to the constitution of this substance, but it seems to me that its recognition is rendered very simple on the supposition of a conjugation; the principal object to be had in view is, therefore, to discover some agent which will dissolve this conjugated compound, and separate the substance into its adjuncts; in how far I have succeeded in this purpose, I am scarcely able to determine. If the somewhat irrelevant question were asked, whether the crystalline substance is contained as such in the blood-corpuscles, existing in it only in a dissolved form, I could not directly affirm that such is the case, for the influence of such forces as light and oxygen, which are necessary to the formation of crystals, is inconceivable without the co-operation of chemical action: hence we might be led to assume that an oxidation had previously taken place. As, however, crystals cannot be formed without the co-operation of carbonic acid, mere oxidation cannot constitute the sole form of metamorphosis of the substance, for carbonic acid must essentially contribute towards the production of the new substance, which is then first rendered crystallisable. It might naturally be supposed that the investigation of this subject would enable us to decide the much disputed question of the interchange of gases in the circulating blood, but the decision of this point is by no means so easy as we might be disposed at first sight to assume; at all events, owing to the small quantity by weight which is taken up by this substance, I have hitherto been unable to obtain any reliable results from my own quantitative determinations; other essential obstacles, moreover, hinder the determination of the gas which is to be absorbed. It must, moreover, be borne in mind that this capacity of the crystalline substance to be changed by the action of oxygen and carbonic acid is not peculiar to this body alone, but pertains without exception to nearly all the protein-bodies, as indeed every careful observer must have noticed, and as I have myself observed in the case of albumen, casein, globulin, &c., when submitted to a similar treatment with oxygen and carbonic acid. All protein-bodies undergo essential alterations in

the open air, as has been observed in numerous instances (we need here only refer to the experiments of Scherer and Panum); but all persons who are conversant with such investigations must be aware of the extreme difficulty of tracing these metamorphoses, owing to the high atomic weight of these bodies. In the meanwhile, I am disposed to regard this crystalline substance as a combination with carbonic acid; and this view seems to derive confirmation, not only from its formàtion in a current of carbonic acid, and its spontaneous production in diseased liver and from putrefaction, but also from the incapacity of the solution to recrystallise after the dried or dissolved crystals have been placed under the air-pump; and finally, from that decided development of carbonic acid which we perceive in the moist crystals in vacuo, and the obviously more abundant development of gas in vacuo when acetic acid has been previously added to the solution. The globulin of the crystalline lens behaves in precisely the same manner, excepting that it is not crystallisable, and does not require the previous application of oxygen for its separation by carbonic acid. When a stream of carbonic acid is passed through the solution of globulin, the latter is precipitated, but this precipitate, on being shaken in pure water and in the open air, again dissolves into a clear fluid, from which the globulin may be again precipitated by carbonic acid. The crystalline substance which has been treated with salt and acetic acid (corresponding to Panum's acid albumen) appears simply to undergo a metameric metamorphosis: it does not separate into several different substances on being coagulated by boiling (as Panum maintained was the case with albumen in the formation of acid albumen), but is rendered far more susceptible towards atmospheric influences than the original crystalline substance.

(45) Addition to p. 396, line 10 from bottom.—Scherer* has, however, recently found a substance in leucæmic blood which appears, from all its reactions, to be nothing else than glutin, and which consequently stands, in a chemical point of view, between the protein-bodies and gelatigenous matters.

It is, moreover, worthy of notice, that the embryo, up to the final period of its leaving the egg, contains no gelatigenous tissue (Hoppe†). Animal cell-walls and nuclei appear never to consist of gelatigenous tissue (Hoppe).

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 321-325.

† Arch. f. pathol. Anat. Bd. 5, S. 174.

(46) Addition to p. 398, line 2 from bottom.—Chondrin, when treated with sulphuric acid, yields, according to Hoppe,* no glycine, but only leucine. If sulphurous acid be passed through a warm solution of chondrin, the latter is at first precipitated, but afterwards undergoes decomposition with a development of ammonia and the formation of leucine and other products. On boiling with alkalies, chondrin is gradually decomposed with a development of ammonia. On treating it with a stronger solution of potash, or on fusing it with hydrated potash, there are formed glycine, leucine, and other products of decomposition. (Hoppe, however, could not find tyrosine.) In the putrefaction of chondrin there are formed, according to Hoppe, leucine and another crystallisable substance, in addition to other products of decomposition. On oxidation with chromic acid, it developes much prussic acid, but neither formic nor acetic acid.

Hoppe, who has more carefully analysed chondrin than any of his predecessors, found 6·28% of salts in the substance in its ordinary state, and only 0·68% in chondrin treated with acetic acid.

The following is his method of preparing this substance: Cartilages are boiled for a short time, so as to effect the partial solution of the perichondrium, and, after its removal, they are cut into thin slices, macerated for some hours in cold water, and then boiled in a modified Papin's digester for 45 minutes or an hour, under a pressure of two or three atmospheres, by which means the greatest part of the cartilaginous substance is dissolved. On cooling the digester to 100°, the fluid is filtered as rapidly as possible, the filtrate evaporated, treated with cold water, the residue again dried, pulverised, extracted with boiling alcohol, and then dried at 120°. To remove the inorganic salts we must precipitate the solution of chondrin immediately after its first filtration with acetic acid, and after decanting the supernatant fluid, we must treat the precipitate with water; after the removal of the salts, it is, however, somewhat difficult of solution in boiling water.

(47) Addition to p. 453, line 7.—Boussingault† has recently attempted to determine the amount of ammonia in the urine by a new method, which depends upon the fact that all the ammonia may be developed from dissolved ammoniacal salts when they are evaporated to dryness in a vacuum with hydrated lime or carbonate

* Journ. f. pr. Ch. Bd. 56, S. 129.

† Ann. de Chim. et de Phys. 3 Sér. T. 29, p. 472.

of soda, at a temperature of from 40° to 50°, while the urea is not decomposed by such treatment. Proceeding in this way, Boussingault found 0·034% of ammonia in the urine of a child aged eight months, and 0·114% in that of a youth. It is, however, very questionable whether the nitrogenous matters of the urine, as, for instance, its coloured extractive matters, which are decomposed far more readily than urea, may not, under these conditions, develope ammonia. At all events it would be remarkable if, after the use of the salts of ammonia, we were to find (as Bence Jones has done) not these salts, but their highest product of oxidation in the urine, while, when these salts have not been taken into the organism from without, the ammonia formed in the body should not be decomposed, but should pass off as such in the urine. Moreover, it is not impossible that the ammonia found by Boussingault may have been formed within the body.

END OF ADDITIONS AND NOTES TO VOL. I.

ADDITIONS AND NOTES TO VOLUME II.

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(1) Addition to p. 30, line 17.—Colin* appears to have made very extensive observations on the secretion of saliva in the solidungula. Amongst other results of his investigations he mentions that the secretion of the two parotids alternates, the parotid of the side on which mastication is going on, secreting at least one-third more than that of the other side; and that when the masticatory process is transferred to the other side, the activity of the first gland very rapidly diminishes, and that of the second as rapidly increases. He did not observe the alternating action in the secretion of the submaxillary glands, which is apparently uniform on both sides. When the animal consumes dry food, there are secreted from 5000 to 6000 grammes of saliva from all the glands in the course of one hour; about 1-3rd or 1-4th more when the animal consumes oats; and 1-5th or 1-4th less when living on succulent roots. The parotids alone yield more than 2-3rds of the whole sum, the submaxillaries only 1-20th, and the sublinguals and mucous follicles the remainder. The secretions of the parotid and submaxillary glands occur almost solely during mastication, and for a short time subsequently; the thick and tough secretion of the other glands of the buccal cavity, which remain moist during abstinence, amount to only 1-37th of the whole. The sight of food excites no perceptible augmentation of the salivary secretion even in fasting animals.

Some very interesting experiments on the influence of the period of secretion on the chemical constitution of the saliva, have been made by Becher and Ludwig.† They found that the solid residue of the saliva diminishes in proportion to the amount which the gland has already yielded; the organic constituents sinking far more rapidly than the inorganic. Fluctuations in the quantity of water in the blood did not disturb this law, as was proved by the examination of saliva collected after one or more venesections; nor was it affected by the injection of chloride of sodium into the blood,

* Compt. rend. T. 34, pp. 327-330.

† Zeitschr. f. rat. Med. N.F. Bd. 1, S. 480-483.

although the quantity of salts in the saliva was somewhat augmented thereby.

(2) Addition to p. 31, line 11 from the bottom.—The more recent carefully conducted experiments of Bidder and Schmidt* have, however, shown that the parotid secretion does not contribute to the action of the mixed saliva. Parotid saliva and buccal mucus do not metamorphose starch, although this effect is rapidly produced by the secretion of the submaxillary glands and the buccal mucus. These enquirers arrived at the same result, namely, that the starch-ferment is only developed by the union of the buccal mucus with the submaxillary saliva, by tying the ducts of the different salivary (the parotid and the submaxillary) glands in dogs.

(3) Addition to p. 36, line 15.—Bidder and Schmidt, under whose superintendence the experiments of Jacubowitsch were instituted, have convinced themselves by later experiments, that the saliva loses its action on starch in the stomach of the living animal. They introduced boiled starch under the most varied conditions, into the stomachs of dogs through gastric fistulæ, and found that after two hours' retention in the stomach, at most only mere traces of sugar could be detected, while externally to the organism this metamorphosis always occurred, even when an excess of gastric juice was added. This perfect suspension of the action of the saliva on starch within the stomach cannot be sufficiently explained either by the comparatively short retention of the starch in the stomach, or by the assumption that the salivary diastase is digested by the gastric juice. For on the one hand the amylacea generally remain a sufficiently long time in the stomach to undergo metamorphosis, and, on the other hand, the gastric juice would also digest the salivary diastase externally to the organism, which is not the case. These results of Bidder and Schmidt may be to a certain degree explained by the assumption, that in these experiments (in which starch was introduced through a fistula, or in the form of very moist starch-paste, through the mouth) only little saliva flowed into the stomach, where it became too much diluted by the gastric juice.

We are, consequently, led by the earlier observations of Bernard, as well as by the more recent investigations of Bidder and Schmidt, to the conclusion, that notwithstanding its energetic action on starch, and notwithstanding its abundant supply, the

* Die Verdauungssäfte und der Stoffwechsel. S. 21.

saliva takes no very important part in the digestion of the amylacea. Hence its principal use in the animal body must be of a mechanical nature. Besides the uses of this nature, mentioned in the text, Bidder and Schmidt believes that one of the main objects of the salivary secretion is its co-operation in the perpetual interchange of the watery fluids within the living organism.

(4) Addition to p. 41, line 15.—Schmidt, who analysed specimens of gastric juice free from lactic acid, found that in nine analyses of the gastric juice (not mixed with saliva) of dogs, the free hydrochloric acid varied from 0·245 to 0·423%, the mean being 0·335%; in gastric juice containing saliva, he obtained in three analyses from 0·1708 to 0·3353%, the mean being 0·2337%; while the gastric juice from the fourth stomach of the sheep yielded as the mean of two analyses 0·1234%. The gastric juice of the sheep always contained a little lactic acid, which, however, was apparently not secreted by the glands in the walls of the stomach, but formed by fermentation from starch.

(5) Addition to p. 45, line 4.—Schmidt, moreover, found that *chloride of ammonium* was constantly present in the gastric juice; its quantity varied in the pure gastric juice of the dog from 0·0372 to 0·065% (the mean being 0·047%), and in the gastric juice mixed with saliva from 0·0276 to 0·084%, while in the gastric juice of the sheep it averaged 0·0475%. The gastric juice (free from saliva) of the dog contains on an average 0·4256% of *fixed chlorides*, while that which is mixed with the saliva contains 0·588%, the addition of the saliva to the gastric juice inducing an augmentation of the chlorides of sodium and calcium; of the latter Schmidt found only 0·0624% in pure gastric juice, while the quantity amounted to 0·1661% in the mixed fluid. The gastric juice (containing saliva) of the sheep contains on an average 0·6% of fixed chlorides.

(6) Addition to p. 46, line 5.—With regard to the *ferment* of the gastric juice, Schmidt obtained it by neutralising the fluid with lime-water, evaporating to the consistence of oil, and precipitating with anhydrous alcohol; this precipitate was then dissolved in water, and thrown down with bichloride of mercury; in the organic matter of this mercury-compound Schmidt found 53·9% of carbon, 6·7% of hydrogen, and 17·8% of nitrogen.

The mean amount of the *organic matters* both in pure and in

mixed gastric juice, was a little above 1·7%, while the mineral constituents averaged 1·0%.

Schmidt found no essential difference in the composition of the gastric juice of dogs, after they had been fed for a long time solely with vegetables, or solely with flesh. It cannot, however, be a mere accidental co-incidence, that the highest numbers for the phosphate of iron were found in four cases after the use of vegetable food.

(7) Addition to p. 53, line 15.—In order to determine the *daily quantity of gastric juice which is secreted*, Bidder and Schmidt employed dogs with gastric fistulæ, which they made to lie on the left side when the secretion commenced, by which means the passage of any part of the gastric juice through the pylorus into the duodenum was prevented: the secretion was, moreover, collected on various days (with a considerable interval between them) and at different periods after the last meal. They collected 823 grammes of gastric juice from a dog weighing 16 kilogrammes, which on the whole was submitted to 14 observations, extending over 12 hours. (These observations of course not being continuous.) Another dog weighing 12 kilogrammes yielded 231 grammes in 4 hours (it having been submitted to 6 observations). In the first case there were 103, and in the second, 115 grammes of gastric juice secreted for each kilogramme's weight of the animal. We may, therefore, assume that the dog yields, at the least, 10% of its weight of gastric juice in 24 hours. We further know that in the healthy state the secretion of gastric juice is for the most part dependent on the ingestion of food, and that some kinds of food excite a more copious flow of this fluid than others. There are some substances, such, for instance, as sugar, aromatics, spirits, and alkalies, which when introduced into the stomach, immediately excite an almost gushing secretion of gastric juice, while other substances, as for instance, animal food, require a far larger quantity of gastric juice for their metamorphosis, in consequence of the much longer time of their retention in the stomach.

(8) Addition to p. 59, last line.—It further follows from the numerous experiments of Bidder and Schmidt, that pure gastric juice considerably exceeds gastric juice mixed with saliva in its digestive power,—a fact obviously dependent on a portion of the free acid of the gastric juice being saturated by the alkaline saliva. They likewise found that the addition of bile to the gastric juice

entirely suspends its solvent action, although the mixture still exhibits a decided acid reaction.

This latter experiment distinctly explains how it is that, when still undigested albuminous matters pass into the intestine, the gastric juice loses all power over them. If there be an acid reaction in the duodenum, this does not depend upon the presence of free hydrochloric acid, but on that of the biliary acids isolated by it. Since these are either very readily resorbed or else are insoluble, we commonly fail to observe an acid reaction in the jejunum even after the use of a flesh-diet.

With regard to the *quantities of albuminous substance* which can be dissolved by definite quantities of gastric juice, I have found that 100 grammes of the fresh gastric juice of the dog are able, on an average, to dissolve 5 grammes of coagulated albumen (this being the mean of eight experiments, in which the extremes were 6·14 and 4·317 grammes). Schmidt, who instituted similar experiments, arrived at a far lower result: as a mean of 27 experiments, he found that 100 grammes of gastric juice dissolved only 2·2 grammes of albumen; the highest number which Schmidt found being 3·95 grammes. The method which I pursued in these investigations was the same as that which I adopted in my experiments with artificial gastric juice. The higher numbers which I obtained were probably dependent on the presence of lactic acid in the fresh gastric juice, while Schmidt only operated on gastric juice in which there was no lactic acid. Since many conditions favouring the solution of the protein-bodies co-operate within the stomach, and since the gastric juice obtained from fistulous openings probably possesses less digestive power than that which is secreted from uninjured stomachs, Bidder and Schmidt very correctly infer that the gastric juice may be able to dissolve a larger amount of albuminous matter than the results of our experiments would seem to show.

Now, if we know the quantity of the gastric juice which is secreted in twenty-four hours (see the preceding page), [and the quantity of albumen which is dissolved by a definite quantity of gastric juice, we can readily ascertain the quantity of albumen which can be daily digested in the stomach. Since a dog secretes about 100 grammes of gastric juice for every kilogramme's weight of its body, that animal would only be able to digest 5$\frac{0}{0}$ of its weight of albumen (reckoned as dry). But it appears from the numerous experiments of Schmidt, that a dog, in order to keep in condition on an exclusive flesh-diet, should take for every kilogramme's

weight of its body 50 grammes of flesh containing 10 grammes of dry albuminates; hence the gastric juice secreted by the dog would only suffice for the digestion of half of the albuminates necessary for the nutrition of the dog,—a result which, paradoxical as it may appear in connexion with the preceding view regarding the digestion of albumen, stands in the most perfect accordance with other observations presently to be described.

(9) Note to bottom of p. 60.—[Gruenewaldt* and Schroeder† have recently published excellent Theses on the human gastric juice, the former taking up its physical and chemical characters, and the latter investigating its digestive powers. Their observations were conducted at Dorpat, under the superintendence of Bidder and Schmidt, on an Esthonian peasant, Catharine Kütt, in whom there was a gastric fistula (the origin of which they could not ascertain) in the left side, at the lower border of the mammary gland, between the cartilages of the ninth and tenth ribs.

The following are the most important results of Gruenewaldt's observations :—

For every kilogramme of bodily weight there are 264 grammes of gastric juice secreted in the 24 hours, the mean daily quantity secreted by this woman being 14·016 kilogrammes, or about 31 lbs., a quantity somewhat larger than that deduced by Schmidt from his experiments on dogs.

The *sarcina* was frequently observed in this fluid obtained from the fistula, both when the stomach was empty and when full, the woman being apparently in perfect health. Hence Gruenewaldt agrees with Virchow,‡ that this organism must not be regarded as a special symptom of a peculiar form of disease.

In relation to the chemistry of this fluid, he found that, when obtained from the empty stomach, it was never acid, but always neutral or slightly alkaline. He gives the particulars of three analyses which were made by Schmidt. In all these cases the secreted fluid was of a very pale reddish tint, moderately acid, formed coagula when boiled, and gave indications of the presence of much sugar, by Trommer's test. When heated it yielded the odour of butyric and metacetonic acid. The spec. grav. of the first specimen was 1·020.

* Succi gastrici humani Indoles physica et chemica, etc. Dorp. Liv. 1853.

† Succi gastrici humani Vis digestiva, etc. Dorp. Liv. 1853.

‡ Arch. f. pathol. Anat. Bd. 1, S. 268.

	I.		II.	III.
Water	954·134		961·251	954·401
Solid constituents	45·866		38·749	45·599
An albuminate coagulating at 100° C. (Pepsin)	0·780			
Sugar, albuminates not coagulating by heat, lactic, and butyric acids, and ammonia....	38·430		31·939	38·659
Chloride of potassium	0·704			
Chloride of sodium	4·263			
Potash (in combination with the organic acids)	0·179	=6·656	6·810	6·940
Phosphate of lime	1·030			
Phosphate of magnesia	0·470			
Phosphate of iron	0·010			

He proves by experiments which are fully described in his Thesis, that the acid which is liberated on the application of heat consists of much butyric acid, with a little metacetonic and, probably, acetic acid; and that the human gastric juice contains *no free hydrochloric acid.* He regards the butyric and lactic acids as products of the metamorphosis of the carbo-hydrates; and, finally, he is persuaded that the acid reaction of the gastric juice, when mixed with food, owes its origin to the organic acids which are contained in or developed from that food.

Schroeder's Thesis is divided into three sections. In the first he considers the action of the human gastric juice on amylaceous matters; in the second, its action on the albuminates, and especially on flesh; and in the third, he briefly notices the part which it takes in the metamorphosis of matter. The only point especially deserving of notice is the description of the analyses of the gastric juice of the same woman, obtained unmixed with food, by irritating the gastric mucous membrane of the empty stomach with pease. An acid, clear gastric juice was then obtained, containing free hydrochloric acid; it would thus appear that in Gruenewaldt's experiments, this acid had been neutralised by the alkali of the saliva.—G. E. D.]

(10) Addition to p. 68, line 7 from bottom.—The differences in the physical characters and in the composition of freshly secreted bile and of bile that has been retained for a long time in the gall-bladder, have been successfully investigated by Bidder and Schmidt. The fresh bile of carnivorous animals (dogs, cats, crows)

varies from a yellow to a yellowish brown colour; while in herbivorous animals (rabbits, sheep, geese) it is green; the colour of the *cystic bile* in animals whose *hepatic bile* is yellow or brown, has, however, always more or less of a tendency to green, and when the animals have not fed for 20 hours or more is of a deep green; while, if examined $2\frac{1}{2}$ or 3 hours after feeding, it is of as light a yellow or yellowish brown colour as the hepatic bile. Since the hepatic bile gradually becomes green on exposure to the air, and the yellow tint may be again restored by deoxidising agents, there can be no doubt that this change of colour depends on oxidation, and that the bile retained in the gall-bladder is impregnated by the circulating blood with so much oxygen as to induce this altered colour.

The prolonged retention of the bile in the gall-bladder induces, however, not only a partial oxidation of this secretion, but also a strong concentration,—a fact which has been established by the numerous observations of Bidder and Schmidt, and has been confirmed by Nasse. The former inquirers found that the fresh hepatic secretion of cats, dogs, and sheep contained on an average 5% of solid constituents, which in the case of cats and dogs rose to 10 or even 20% in the cystic bile, according to the duration of its retention in the gall-bladder: in sheep, on the other hand, the amount only rose to 8%; in rabbits, whose fresh bile contains only 2% of solid constituents, the amount in the cystic bile may rise to 15%. The fresh bile of geese and crows contains about 7% of solid matters, which in the cystic bile of the former may rise to 20%, and in that of the latter even to 25%. The bile, therefore, restores to the blood and lymph a greater or smaller quantity of water, according to the duration of its retention in the gall-bladder.

(11) Addition to p. 78, line 18.—[The experiments of Bidder and Schmidt, which are here briefly referred to, are given in considerable detail in the new edition.—G. E. D.]

Bidder and Schmidt have obtained the following results regarding the absolute quantity of the bile secreted in 24 hours by the animals on which they experimented. For one kilogramme's weight of the animal there were secreted—

	In cats.	In dogs.	In sheep.	In rabbits.	In geese.	In crows.
Of fresh bile	14·500	19·990	25·416	13·684	11·784	72·096
Of solid constituents in it ...	0·816	0·988	1·344	2·47	0·816	5·256

Nasse,* who made very numerous observations upon a single dog, obtained rather a higher mean number for the amount of bile than Bidder and Schmidt, who made numerous experiments on different dogs; there being, according to Nasse, 21·025 grammes of fresh bile, containing 0·746 of a gramme of solid constituents, secreted in 24 hours for each kilogramme's weight of the animal.

Experiments made on dogs led to precisely the same results as those upon cats [mentioned in vol. ii, p. 79]; the secretion reaching its maximum between the thirteenth and a half and the fifteenth and a half hour after the last meal. Greater fluctuations were, however, observed in the gradual augmentation of the biliary secretion in dogs than in cats.

The circumstance that the quantity of secreted bile, after attaining its maximum in the fifteenth hour after the last meal sinks with extraordinary rapidity, and even below the number which expresses the biliary secretion in the first hour after taking food, was confirmed by Bidder and Schmidt in their still more numerous experiments on dogs.

The same observers have likewise convinced themselves that when animals remain for a longer period than 24 hours without food (48, 72, 168, or 240 hours), the biliary secretion continuously diminishes, the daily diminution being, however, gradually less in proportion to the time that has elapsed since food was last taken. Thus, for instance, in cats, after 10 days' fasting, the biliary secretion amounted to only the fourth part of the quantity yielded in the 24 hours succeeding the last meal.

It was repeatedly observed by Bidder and Schmidt, and the observations have been confirmed by Nasse, that animals with permanent biliary fistulæ generally have a ravenous appetite. This circumstance may assist us in determining the question, whether the biliary secretion bears a definite proportion to the quantity of food that is taken. The question has been decided in the affirmative by the experiments of the first-named inquirers, and a series of observations by Nasse also confirm this view. Thus, for instance, Bidder and Schmidt found that when cats were over-fed, the quantity of bile that was secreted exceeded by one-fifth the quantity which is commonly secreted by a cat after a moderately abundant meal. In these cases the augmented secretion of bile was, moreover, accompanied by an augmentation of its solid constituents.

* Commentatio de bilis quotidie a cane secreta copia et indole. Progr. Marburgense, 1851.

From the preceding observations it might be expected that the *nature of the food* would exert a certain influence on the amount of the hepatic secretion; and this expectation has been thoroughly confirmed by the experiments of Bidder and Schmidt, and of Nasse. A *flesh-diet* induces a far more abundant secretion of bile than vegetable, amylaceous food. Thus, for instance, Nasse's dog, when fed on bread and potatoes, daily secreted 171·8 grammes of bile, containing 6·252 grammes of solid matter; but when fed upon flesh it secreted in the same period 208·5 grammes of bile, containing 7·06 grammes of solid matter. In admirable co-incidence with these experiments are those instituted by Bidder and Schmidt on cats, which, when fed on pure *fat*, secreted no more bile than if they had been completely deprived of food for the same time. An *exclusive* fatty diet, therefore, exerts no influence on the secretion of bile. In Nasse's case, however, an abundant addition of fat to the ordinary food of the dog occasioned a marked augmentation of the biliary secretion.

In repeated experiments both on cats and dogs, Bidder and Schmidt found that, after the copious ingestion of water, the quantity both of the bile and of its solid constituents was increased. After water has been freely taken the bile is certainly somewhat richer in water than normal bile, but with this water there is at the same time secreted a larger amount of solid constituents than is usually eliminated by the liver. This result has also been confirmed by Nasse. Hence it is not surprising that slight variations are perpetually being observed in the ratio of the water to the solid constituents of the bile secreted in definite times; and hence, too, it is that in the numerous tables drawn up by Bidder and Schmidt, all influences on the hepatic secretion are far more distinctly and precisely reflected on the amount of the solid constituents than on that of the fresh aqueous bile. Nasse lays special stress upon the point, that the variations which we observe in the quantity of the solid constituents of the bile are chiefly induced by the organic matters, while the mineral substances secreted in definite times remain nearly constant.

After large doses of *carbonate of soda,* Nasse observed a considerable diminution of the secretion of bile, and especially of the solid constituents. *Alcohol* caused an augmentation of the fluid bile, but a diminution of its solid constituents.

Finally, Nasse entirely coincides with Bidder and Schmidt, that *disease* (namely, febrile excitement) has an extraordinary effect in diminishing the quantity of the secreted bile.

We must not overlook this opportunity of noticing the observations which Bidder and Schmidt have made regarding the *intermittent emptying of the gall-bladder*. Magendie first made the observation, that, after prolonged fasting, the gall-bladder is distended with very concentrated bile; Bidder and Schmidt have now convinced themselves that the gall-bladder does not empty itself immediately after the ingestion of food, but 2½ or 3 hours later; the mere distension of the stomach cannot therefore occasion the discharge of the contents of the gall-bladder. It must not, however, be inferred from this circumstance that all animals possessing a gall-bladder only effuse bile into the intestine during the period of digestion, and that at other times all the secreted bile is accumulated in the gall-bladder. For far more bile is secreted during the intervals between the individual meals than could be held in the gall-bladder; thus, for instance, the gall-bladder of a full-grown cat cannot contain more than about 3 grammes of bile, although the animal secreted in 24 hours from 30 to 32 grammes of bile, and therefore far more than could be collected in the gall-bladder, even with four or five emptyings after the ingestion of food. And the fact is still more strikingly shown in rabbits; the gall-bladder of a rabbit weighing 1 kilogramme can contain at most 0·469 of a gramme of bile; but since this animal sends 7 grammes of bile into the intestine in one hour, it is hence still less possible to conceive that all the bile must take its course through the gall-bladder.

(12) Addition to p. 105, line 14.—After so many fruitless attempts to establish on incontestible grounds the co-operation of the bile in the *digestion of the fats*, Bidder and Schmidt* have at length succeeded in submitting the question to the most exact proof. We shall follow these investigators through the different steps of the experimental proof by which they established the point. Experiments on dogs, in which they formed fistulous openings into the gall-bladder after having previously tied the ductus choledochus, showed that the bile which is poured into the intestine is devoid of any influence on the digestion of albuminous matter and of starch. Animals, which had been thus operated on, digested the same quantities of albuminous food as sound animals in which the bile could run unimpeded into the intestine, and in each case the process seemed to be equally perfectly performed. Precisely the same was observed in regard

* Verdauungssäfte und Stoffwechsel. S. 215-234.

to amylaceous food; but the case was very different when the quantities of fat were compared with one another which were retained in the body and applied to the purposes of life by the animals that had been operated on and by the healthy animals. It was ascertained by Boussingault (see vol. i, p. 255), and the fact has been confirmed by Bidder and Schmidt, that the animal organism is only able to absorb a definite, and indeed a somewhat small quantity of fat from the intestinal canal. Several experiments on cats have shown that the full-grown animal is at most able to take up 0·6 of a gramme of fatty food for every kilogramme of its weight during the 24 hours, while young animals absorb as much as 0·9 of a gramme. Similar experiments with a dog (which weighed 5 kilogrammes) showed that this animal had resorbed 446·9 grammes of fat in a week; consequently, every kilogramme's weight of the animal would be able to digest at least 0·465 of a gramme of fat in one hour, when plentifully supplied with that substance. These animals, however, absorbed much less fat when the passage of bile was entirely excluded from the intestine; in three series of experiments on these animals it was found that in one case, where the access of bile was prevented, for every kilogramme of the animal's weight only 0·093 of a gramme of fat was absorbed, in another case 0·065 of a gramme, and in the third case 0·21 of a gramme. It is very clearly seen from these experiments, that a certain quantity of fat will be absorbed independently of the presence of the bile, although this is $2\frac{1}{2}$ times less in the most favourable cases than the amount of fat which is absorbed in conjunction with the secretion of bile. The opposite experiment of Blondlot,* in which he could scarcely detect a trace of fat in the excrements of a dog having a biliary fistula, and which had been fed on very fat food, has been, for various reasons, and perhaps correctly, referred by Bidder and Schmidt to the fact that a free passage through the Ductus choledochus may probably have been re-established in the animal. The participation of the bile in the digestion of fat must, therefore, be considered as settled beyond a doubt, although it cannot be wholly denied that a small portion of the fat may be resorbed independently of the co-operation of the bile.

As it is well known that the white colour of the chyle is mainly owing to the amount of fat which it contains, the colour of the chyle contained in the lacteals was observed after the bile had been excluded from the intestine; but this experiment was attended by

* Essai sur les fonctions du foie et de ses annexes. Paris, 1846, p. 52.

different results. Brodie,* as well as Tiedemann and Gmelin,† thought that they had convinced themselves that after tying the common bile-duct, the lacteals contained a colourless, transparent fluid, notwithstanding the use of fat food, whilst Magendie,‡ and more recently, even Lenz,§ in connection with Bidder and Schmidt, have seen the chyle appear milk-white under similar relations. If it maybe *à priori* anticipated that we cannot form a very definite opinion of the more or less white colour, or of the greater or less transparency of the chyle contained in the lacteals, the uncertainty of this mode of observation must be doubly manifest to all those who have frequently observed the lacteals in animals which have been killed immediately after feeding. Hence it follows that, as we have already seen, even when the bile is excluded, a portion of the fat is resorbed, and renders the chyle more or less whitish. The quantitative determination was here the only way of deciding the question with certainty, and this was, therefore, the course which Schmidt pursued. In the chyle obtained from the thoracic duct of dogs with biliary fistulæ, he found on one occasion 0·834% of fatty acids mixed with other organic substances, and on another occasion 0·190% of free fat together with 0·113% of fatty acids, while the chyle of a healthy dog, that 8 hours before its death had been fed upon beef, contained 3·244% of free fat, with 0·058% of fatty acids. While the differences in the amount of fat in these two kinds of chyle are so great, the other constituents were found to fluctuate very slightly in their quantitative relations. Moreover, this experiment perfectly confirms the fact which had been otherwise established, that the bile essentially contributes to the absorption of fat.

If it be rendered tolerably evident by these experiments, that the bile is indispensable to the absorption of fat into the juices of the animal organism, its mode of action in this process still remains unexplained: and this result must appear the more striking, seeing that direct experiments instituted with fat and bile afford no clue to the explanation of the mode of action. The bile possesses in a far less degree than the pancreatic juice the power of forming an emulsion, and even if it did possess this property in a well-marked degree, the resorbability would be by no means explained by the extreme comminution of the fat; for since the coats and cells of the

* Quarterly Journal of the Sciences and Arts. 1853, Jan.

† Die Verdauung nach Versuchen. Bd. 2, S. 24-48.

‡ Précis élémentaire de Physiologie. T. 2, p. 117.

§ Op. cit. p. 58.

intestine are continuously permeated with aqueous moisture, and can never be dry at any point, we cannot understand, from a physical point of view, how the oily fat can penetrate these membranes. Hence it has been assumed that the fat is saponified by the alkali of the bile; but since the greater part of the chyle-fat is unsaponified fat, we are compelled either to withdraw altogether from this hypothesis, or to assume with Moleschott,* that the fat is saponified in the intestine (by means of the pancreatic fluid), but is again liberated in the lymphatics. This latter view, independently of its teleological improbability, can hardly be accepted when we consider that after the use of fatty food, mere traces of fatty acids are found in the intestinal canal, that unsaponified fat is recognisable even in the epithelium and cells of the villi, and that, according to Schmidt's experiments, the exclusion of the bile renders the chyle very deficient in free fat, while it does not affect its quantity of fatty acids. Lastly, the bile possesses so very slight a solvent power (none whatever, according to Bidder and Schmidt) for neutral fats (and even for the fatty acids it would appear from the experiments of Lenz, not to be very considerable), that the bile which is secreted would be perfectly insufficient to dissolve the whole of the fat which is resorbed. It has been consequently supposed that individual parts of the inner intestinal surface may be specially capable of absorbing fat, and that fat alone can penetrate through them; but in that case the assistance of the bile in the resorption of the fat would appear to be altogether superfluous. But since the bile has been shown to be necessary to this object, nothing in fact remains but to assume that the bile induces a modification in the relations of adhesion between the oleaginous fluid and the moist watery membranes, by which the transmission of the fat through these membranes is effected. The theory of the physical relations of different kinds of fluids to different membranes has been as yet so little studied, that such an assumption as the above is by no means inadmissible; indeed we find that Bidder and Schmidt performed an experiment which indicates with tolerable distinctness the existence of such a relation; they plunged two glass capillary tubes in oil, having previously moistened the interior of one of them with bile; the oil rose far higher in the tube moistened with bile than in the other, either when it was perfectly dry or when moistened with a saline solution. This mode of explaining the absorption of fat has been established beyond all doubt by the

* Physiologie des Stoffwechsels Erlangen, 1851, S. 209.

accurate experiments of Wistingshausen* (conducted under Schmidt's superintendence), on the relations of the fats when mixed with the acids of the bile to endosmosis and capillary attraction.

(13) Addition to p. 81, line 20.—Moleschott has recently instituted a series of carefully conducted experiments on frogs in relation to this point. Like Kunde, he extirpated the liver; but succeeded in keeping the animals alive for a longer period. He could not succeed in detecting a trace of the resinous acids or of the pigment of the bile either in the blood or in the lymph, or in the flesh, or in the urine of the frogs on which he operated. It may, therefore, be regarded as an established fact, that the essential constituents of the bile are primarily formed within the liver.

(14) Addition to p. 112, line 16.—The specific gravity of the pancreatic fluid is liable to considerable variations (Ludwig and Weinmann†), since the amount of its solid constituents varies inversely with the time during which the secretion has been going on; Frerichs, who examined a very dilute pancreatic juice, determined its specific gravity at 1·008 or 1·009, while Bidder and Schmidt found the specific gravity of a thick viscid specimen which they were investigating to be 1·0306.

In correspondence with this density of the pancreatic juice, Schmidt found that on one occasion it contained 9·92%, and on another 11·56% of solid constituents; in the former case there was 9·04 of organic matters, and 0·854 of ash which contained 0·736 of chloride of sodium, the remainder being chiefly bibasic phosphate of soda.

(15) Addition to p. 114, line 20.—The quantity of the pancreatic fluid varies very much in different animals; according to Colin‡ it does not stand in a direct ratio to the volume of the gland. While the pancreas of the ox and of the horse yields 260 or 270 grammes in an hour, that of the swine, which is about half the size, yields only 12 or 15 grammes in an hour.

The recent observations of Bidder and Schmidt on the pancreatic juice of the dog differ considerably from those of Bernard [quoted in the text]. They found that a strong dog (weighing 20

* Dissert. inaug. Dorp. Livon. 1851.

† Dissert. inaug. Zurich 1852.

‡ Compt. rend. T. 34, p. 85.

kilogrammes) secreted 7·86 grammes in 8 hours and a quarter, there being 1·614 grammes secreted in the first hour, while in the eighth there was only 0·73 of a gramme. We must, however, observe that the secretion was only collected from the lower and larger duct, while the course of the fluid into the intestine through the upper and smaller duct was not impeded. From these observations on the dog, Bidder and Schmidt calculate that an adult man, weighing 64 kilogrammes [or about 10 stone], secretes 150 grammes in 24 hours.

Ludwig and Weinmann found in a series of experiments, which extended over 7 days, and included 37 observations, that a dog for every kilogramme's weight secreted 35·184 grammes of pancreatic fluid in 24 hours. The amount is, however, liable to considerable variations; prolonged hunger, vomiting, and operations on the animal diminish the amount, while the ingestion either of solids or fluids increases it. The quantity increases very rapidly after water has been taken; in two experiments the secretion attained its maximum in 12 or 13 minutes after drinking.

(16) Addition to p. 115, line 3.—Bidder and Schmidt have likewise shown that the matter on which the sugar-forming power of the pancreas depends, exists preformed in the fresh juice, and is not, therefore, formed as in the saliva, by the mixture of different fluids, and that it maintains its efficiency far below the temperature of the animal body, and does not even lose this power of metamorphosis when it has remained for 24 hours at a temperature of 18°, while its action on starch is not affected either by the bile, the gastric juice, or free acids.

In order to institute a comparison between the amount of force exerted on starch by the saliva and by the pancreatic juice, it would be absolutely necessary to make an accurate quantitative determination of the amount of starch which may be metamorphosed by equal quantities of the two kinds of juices; but, unfortunately, determinations of this nature, however important they may be in other respects, have not been successfully accomplished. We believe, however, that we should no more over-estimate the metamorphosing action of the pancreatic juice than that of the saliva, for although the action of the pancreatic juice may be somewhat stronger than that of the saliva, it is a striking fact, that we generally find many unchanged, or at most merely transversely contracted starch-globules in the excrements of herbivorous and even of ruminating animals (even when they

have been sparingly fed upon amylaceous food for some days before they were killed). Since, on the other hand, Bidder and Schmidt have made the observation in the case of a sheep having a fistula in the abomasum, that only a small quantity of starch was found in its fourth stomach, we must necessarily regard the metastatic force of the pancreatic juice as somewhat limited. (I am bound to observe, that the presence of starch is always recorded in my journal in reference to my various examinations of the contents of the stomachs of ruminating animals.)

The action of the pancreatic juice does not, moreover, appear to extend very far into the intestine. According to Bidder and Schmidt, it seems wholly to disappear in the upper half of the intestinal canal; at all events the contents of the intestine are unable beyond that point to develope butyric acid from butter, which is a property of this juice.

Colin has already specially noticed the fact, that the amount of the secretion does not stand in a direct relation to the volume of the pancreas, and hence we should be cautious in drawing any conclusion as to the functions of this gland from the volume of the pancreas in different animals; besides, the volume of this gland is so different in different animals living on the same kind of food, that nothing either for or against any view can be deduced from the size of the pancreas: formerly it was generally assumed that the pancreas was on an average by far more voluminous in the herbivora than in the carnivora, but in the rabbit, for instance, the weight of this gland amounts to 1-600th part of the bodily weight. Bidder and Schmidt, who made the latter observation, assign to the carnivora the more voluminous pancreas, but this again is not strictly true, for while in cats, for instance, the weight of this gland amounts to 1-300th part of their bodily weight, in the beaver it amounts to 1-30th. (E. H. Weber).

(17) Addition to p. 121, line 12.—[The following are the most important facts which Lehmann has added to the section on the Intestinal Juice; they are derived from Bidder and Schmidt's work, and from Zander's Thesis.—G. E. D.]

Fresh, pure intestinal juice has hitherto been only examined by Bidder and Schmidt,* and (under their superintendence) by Zander:† it is a colourless, ropy, viscid fluid, which is invariably alkaline; the alkalinity, however, varies in different animals, and in

* Verdauungssäfte und Stoffwechsel. S. 260-282.

† Diss. inaug. Dorp. Livon. 1850.

different parts of the intestine; but no definite rule can be laid down on this subject.

The juice, after the removal, by filtration, of the morphological elements mentioned in the text (see p. 119), contains no trace of albumen, and, therefore, does not coagulate either on boiling or on the addition of acetic acid: alcohol of $85\frac{0}{0}$ throws down white flakes which redissolve in pure water; their solution is precipitated by acetate of lead, but not by the mineral acids, or by bichloride of mercury: the acetate-of-lead precipitate dissolves readily in acetic acid.

According to Bidder and Schmidt, the filtered intestinal juice of dogs contains from $3{\cdot}042\frac{0}{0}$ to $3{\cdot}467\frac{0}{0}$ of solid substances.

Zander found $3{\cdot}9\frac{0}{0}$ of solid constituents in a specimen of intestinal juice containing bile and pancreatic fluid; amongst the solid constituents there were 2·5 parts soluble in alcohol (glycocholate and taurocholate of soda), and 1·4 parts insoluble in alcohol (taurine, pancreatic fluid, and intestinal juice); the unfiltered juice contained $0{\cdot}8\frac{0}{0}$ of epithelium, &c.

Bidder and Schmidt infer from the following observation, that the pure gastric juice must be a tolerably diluted fluid. The filtered intestinal contents, in which there are $3{\cdot}8\frac{0}{0}$ of solid constituents, consist not only of the true intestinal juice, but also of gastric juice, bile, and pancreatic fluid; the gastric juice has about the same concentration as the fluid intestinal contents; but the bile of the dog contains $5\frac{0}{0}$, and the pancreatic juice $10\frac{0}{0}$ of fixed substances; hence the intestinal contents could not attain to such a high degree of dilution, unless the true intestinal juice were an extremely aqueous fluid.

It is obviously impossible to form any certain determination regarding the *quantitative relation* of this secretion. Bidder and Schmidt calculated from the contentration of the mixed intestinal juice (that, namely, containing bile, gastric juice, and pancreatic fluid), and that of the gastric juice, the bile, and the pancreatic fluid, that the pure intestinal juice must contain about $15\frac{0}{0}$ of solid constituents, and that, consequently, that an adult man (weighing 64 kilogrammes or 10 stone) secretes in 24 hours about 300 grammes of intestinal juice.

The quantity of the secretion naturally varies according to the period of digestion. In the dog, in which an intestinal fistula was formed in the middle of the small intestine, the following remarkable facts were observed by Bidder and Schmidt. This secretion flowed most abundantly from the fistula 5 or 6 hours after a meal;

and its quantity was considerably increased very soon after drink had been taken: however, the most singular circumstance is, that the intestinal juice shows the same concentration as before the ingestion of the fluid; hence we must conclude with Schmidt, that the drink is absorbed in the stomach and in the upper part of the small intestine, and that the water, which thus finds its way into the blood, increases the intestinal juice in common with the other secretions.

With regard to the *functions* of the intestinal juice, it seems to a certain degree to unite in itself the powers of the gastric and pancreatic fluids. For it is established by the numerous experiments of Bidder and Schmidt, that this fluid can dissolve and render fit for resorption not only *starch*, but also *flesh and other protein-bodies*. Starch (in the form of paste) when introduced into previously cleared and tied loops of gut, was usually converted in the course of three hours into a thin fluid mass, which no longer gave the well-known reaction with iodine. Starch-paste and intestinal juice, when mixed together and exposed to a temperature of from 35° to 40°, assumed a thin fluid condition in the course of a quarter of an hour, and the mixture was then found to be rich in sugar.

In a similar way pieces of flesh or of coagulated albumen were introduced into tied loops, and in the course of from 6 to 14 hours they were found to be for the most part or entirely digested. It was also shown by experiments, made externally to the organism, that pure alkaline intestinal juice, as well as that secretion when mixed with bile and pancreatic juice, possesses the power of dissolving protein-bodies. Pure intestinal juice dissolved in the course of 6 hours from 36·4 to 40·7 % of the flesh digested in it, and very similar ratios were observed when intestinal juice mixed with bile and pancreatic fluid was used. Hence it follows that bile and pancreatic fluid, which impede the digestion of the albuminates by the gastric juice, do not in any way interfere with the digestive powers of the intestinal juice.

We may here refer to a fact which has been previously mentioned (see p. 502 of this volume), namely, that a very large amount of albuminates passes undigested from the stomach, and that the quantity of gastric juice which is secreted is not sufficient to effect the solution of the protein-matter necessary for nutrition; and from this we should obviously conclude that nature has provided some other digestive agent as a solvent for the protein-bodies in addition to the gastric juice; and the same remark applies to the saliva and

pancreatic juice in relation to the digestion of starch. We have seen (see p. 514 of this volume) that the pancreatic juice disappears, that is to say, is again absorbed before it reaches the middle of the small intestine, and yet we find that starch is readily converted into sugar below this point. These two properties of the intestinal juice are therefore both directly and indirectly proved.

(18) Addition to p. 126, line 18 from bottom.—Schmidt propounds the question—to what extent is the bile decomposed in its passage to the middle of the small intestine? In order to decide this question, the quantity of the biliary acids precipitated by acetate of lead was compared with the taurine that is already formed, and which was calculated from the amount of sulphur in the fluid freed from an excess of lead: in 100 parts of the intestinal contents, there were 2·48 parts of fats and biliary acids soluble in ether, 2·021 parts of insoluble biliary matters (cholic, glycocholic, and taurocholic acids), and 0·143 of taurine. Since the latter is equivalent to 0·622 of pure bile-substance, it follows that almost half of the bile effused into the intestinal canal is decomposed before it reaches the middle of the small intestine.

(19) Note to p. 126, 6 lines from the bottom.—[The fæces have been submitted to chemical examination during the last few months by Wehsarg,* Ihring,† and Marcet.‡—G.E.D.]

The following are the most important points in Wehsarg's Thesis:—The *colour* of the normal fæces varies with the food; on a mixed diet they are of a yellowish-brown tint, on a flesh-diet they are much darker, and on a milk-diet quite yellow. On exposure to the air the colour usually becomes darker, but never red. Very dilute nitric acid, when added in sufficient quantity, always communicates a red colour to the fæces.

The *odour* almost entirely disappears on drying, or, at all events, becomes less disgusting. It varies with the kind of food. As a general rule the odour is most intense when the stools follow one another rapidly.

The *consistence* seems to depend chiefly on the constitutional

* Mikroskopische und chemische Untersuchungen der Fæces gesunder erwachsener Menschen. Inaug.-Abhandl. Giessen, 1853.

† Mikroskropisch-chemische Untersuchungen menschlicher Fæces unter verschiedenen pathologischen Verhaltnissen. Inaug.-Abhandl. Giessen, 1853.

‡ Proceedings of the Royal Society, June 15th, 1854. Vol. 7, p. 153.

relations of the person; but it is considerably influenced by bodily exercise.

The *reaction* is most commonly acid, but not unfrequently alkaline or neutral.

The number of observations made by Wehsarg was 27; and in 17 of these cases the fæces were those of the 24 hours.

The *quantity* of the daily fæces is very variable; the mean of these 17 observations being 131 grammes (or about 4·6 ounces), the largest and smallest quantities being 306 and 67·2 grammes respectively. This irregularity did not seem in any way connected with an excess of undigested matter. It may be laid down as a general rule, that when the food passes rapidly through the intestine, the daily quantity of the fæces is larger then when it is retained for a longer time in the intestine. In proportion to the rapidity with which the stools follow one another, there is a smaller relative, but larger absolute amount of solid matters. There is no definite relation between the amount of fæces and the bodily weight; the quantity of the fæces seems rather to be connected with the digestive power of the individual.

The fæces, when in a formed or half formed state, contained (taking the mean of 17 observations) 73·3% of water and other matters which were volatile at 120° C., and 26·7% of solid constituents; the latter varied from 17·4 to 31·7%.

The absolute quantity of solid matters discharged in the 24 hours averages 30 grammes, the extremes being 57·2 and 16·3 grammes. No safe inference can be drawn from the consistence of the fæces as to the amount of water and volatile matters that they contain.

The amount of *undigested matters* varies very much in different cases; the mean quantity in 10 observations was 3·4 grammes, or 8·3%, the extremes being 8·2 grammes and 0·81 of a gramme.

A microscopic examination always exhibits remains of the food that has been taken. We commonly meet with vegetable cells and hairs, and spiral vessels in abundant quantity. Muscular fibres coloured yellow and corroded by the bile, but still retaining distinct striation, are constantly found. Wehsarg mentions, as of constant occurrence, "a finely comminuted fæcal matter," which appears to be granulo-cellular, but whose structure cannot be distinctly made out; it certainly, however, contains partially destroyed epithelium. Starch is often found. Crystals of ammonio-phosphate of magnesia are always present when the evacuation is neutral or alkaline. Amorphous fat is a constant constituent of

the fæces; but Wehsarg never observed crystals of cholesterin: connective tissue was only noticed after a very abundant flesh-diet.

The *ether-extract* of the fæces varied extremely with the nature of the food. After a very fatty diet it rose to 31·2 grammes, or 58·2$\frac{0}{0}$ of the dried mass; the mean was 11·5$\frac{0}{0}$, and the minimum 8·5$\frac{0}{0}$. It consists for the most part of a waxy fat.

The *alcohol-extract* was found to amount (as the mean of 3 observations) to 15·6$\frac{0}{0}$, and it may rise to double this quantity in diarrhœa. After drying this extract (which when cold forms a dark brownish-red mass) in the air-bath Wehsarg could only once detect the presence of bile in it with certainty, although he often got doubtful indications; and on the addition of nitric acid to fresh fæces there was only twice an undoubted manifestation of the evidence of bile-pigment. Hence his observations confirm the view, that as a general rule no bile occurs in an unchanged state in the fæces.

The *water-extract* is a brownish-black mass, which always undergoes decomposition on drying. Its average quantity is about 20$\frac{0}{0}$ of the dry fæces.

The quantity of *salts* contained in the fæces, as compared with that in the urine, is very small. Mere traces of sulphuric acid and chlorine, and often not even a trace, are to be found, unless when large quantities of these substances have been introduced into the system. Chlorine, is, however, more frequently found than sulphuric acid.

The salts which are precipitable by ammonia vary in different individuals. The mean of 7 observations was 4·10$\frac{0}{0}$, the maximum being 6·90, and the minimum 1·73$\frac{0}{0}$. After a dose of sulphate of magnesia, this number may rise to 20·50$\frac{0}{0}$. The great mass of these salts is phosphate of magnesia, and associated with it is a small quantity of phosphate of lime with a little iron.

It appears, from Marcet's experiments, that healthy human excrements contain:—

1. A new organic substance, possessing an alkaline reaction, which its discoverer names *excretine*. In its pure state it appears in circular groups of crystals, which have the form of acicular four-sided prisms, and polarise light very readily. It is very soluble in ether, cold or hot, but sparingly soluble in cold alcohol; it is insoluble in water, and is not decomposed by dilute mineral acids. It fuses between 95° and 96° C., and at a higher temperature burns away without inorganic residue. It does not

dissolve when boiled with a solution of potash. It contains nitrogen and sulphur, though in small proportions. The products of its decomposition have not yet been investigated. Marcet considers that it exists for the most part in a free state in the excrements, and constitutes one of their immediate principles. As to its source, he observes that it appeared in excess when a considerable quantity of beef had been taken, and in less than the usual quantity in a case of diarrhœa attended with loss of appetite; but none could be directly obtained from beef on subjecting it to the same process of extraction as fæces; neither could it be found in ox-bile, the urine, or the substance of the spleen.

2. A fatty acid having the properties of margaric acid, but not constantly present. He is uncertain whether the margaric acid in the fæces is free, or combined with excretine, but he is disposed to conclude that the neutral fats are decomposed in the intestinal canal, and their acid set free. Not having been able to discover stearic acid in human evacuations, he supposes that what is contained in the fat taken in the food must be converted into margaric acid in its passage through the alimentary canal.

3. A colouring matter similar to that of blood and urine.

4. A light granular substance, which he is inclined to regard as a combination of phosphate of potash and a pure organic matter.

5. An acid olive-coloured substance, of a fatty nature, which he names *excretolic acid.* It fuses between 25° and 26° C., and at a higher temperature burns without residue. It is insoluble in water and in a boiling solution of potash, is very soluble in ether, and in hot alcohol, and slightly so in cold water. He believes that it is combined in the excrements in the form of a salt with excretine or a basic substance closely allied to it.

6. No evidence of butyric or of lactic acid was obtained.

The fæces of various animals yielded the following results:—

1. The excrements of carnivorous mammals, viz., the tiger, leopard, and dog (fed on meat) contain a substance allied in its nature to excretine, but not identical with it. They contain no excretine, but yield butyric acid, which is not present in human excrements.

2. The excrements of the crocodile contain cholesterin, and no uric acid, while those of the boa yield uric acid, and no cholesterin. [It is probable that the semi-solid urine and the excrements were not duly separated in this experiment.—G. E. D.]

3. The fæces of herbivorous animals, viz., the horse, sheep,

dog (fed on bread), wild boar, elephant, deer, and monkey, contain no excretine, no butyric acid, and no cholesterin.

Ihring has examined the evacuations after the use of chloride of sodium, Nauheimer water, and of preparations of iron, and in cases of intestinal tuberculosis, bilious diarrhœa, &c., and has likewise submitted to investigation the contents of different parts of the intestinal contents in a patient who died from a chronic affection of the stomach. We must refer to his thesis for further particulars.—G. E. D.]

(20) Addition to p. 148, line 14.—A solid margarin-like fat has very frequently been found in the excrements in diabetes by Simon,* Heinrich,† and others. I have, however, not succeeded in finding a decided augmentation of fat in the cases in which I have examined the excrements of diabetic patients. The loss of fat through the intestine is therefore, at all events, not a constant symptom in diabetes.

(21) Addition to p. 192, 8 lines from the bottom.—Liebig‡ has recently adduced new and striking proofs in support of the latter view. Water absorbs only 0·925% of its volume of oxygen, whilst, according to Magnus, from 10 to 13% may be taken up by the blood; this greater force of absorption in the blood can only depend upon certain constituents, and principally, as we know, upon the red corpuscles; only from 1-14th to 1-11th of the oxygen which is absorbed by the blood, and which varies from 10 to 13%, can be absorbed mechanically, that is to say, by the water, or can consequently exist free in the blood; the remaining oxygen, that is to say from 13-14ths to 10-11ths, must therefore be fixed by certain blood-constituents; but this is only conceivable through the agency of some chemical attraction, however slight that may be. The chemical combination of oxygen with the constituents of the blood may be very loose and entirely analogous to the combination in which the carbonic acid exists in the blood, as already described (in vol. i, p. 439). The mechanical solution of a gas is entirely dependent upon the pressure which it has to sustain; if a definite quantity be absorbed independently of external pressure, and if this amount stands in a direct proportion to any definite constituent of the fluid, the increase in the

* Beiträge u. s. w. Bd. 1, S. 408.

† Häser's Arch. Bd. 6, S. 306.

‡ Chem. Briefe. 3 Aufl. S. 419-423 [or Letters on Chemistry, 1851, pp. 332-335.]

absorbing power of the fluid cannot be referred to any cause but chemical attraction. Although, in the case of the oxygen, we are not so well acquainted with the matters which retain it, as with those which are able to fix the carbonic acid in the blood (alkaline carbonates, phosphates, &c.), the proposition is almost equally established for both cases, that the excess of carbonic acid and oxygen which the blood is able to absorb beyond the amount which corresponds to the quantity of water which it contains, must be present in the blood in a state of chemical combination. We have already endeavoured to show (in vol. i, p. 439) that the possibility of breaking up such an unstable combination by the aid of other indifferent gases (as hydrogen, &c.) furnishes no evidence against the fact that the expelled gas has been chemically combined. Liebig is therefore certainly in the right when he advances the proposition, that a gas can only be considered as mechanically absorbed when its quantity increases and diminishes in proportion to the external pressure. We think we are justified in concluding with Liebig, that the quantity of oxygen which may be absorbed by the blood is constant in amount, and to a certain extent independent of external pressure,—an opinion which is based partly upon the fact, that the respiratory process is carried on nearly the same, both at very great heights and at the level of the sea, and that no more oxygen is absorbed even in an air very rich in oxygen than in the ordinary atmosphere.

In addition to these physical proofs in favour of the chemical absorption of the oxygen in the blood, I may perhaps be permitted to refer to the following experiments, instituted by myself, with the pure crystalline substance of the blood, although they can scarcely be said to furnish any conclusive result. A perfectly limpid saturated solution of pure blood-crystals, which was not precipitable either by nitrate of silver or by basic acetate of lead, and which was of a beautiful pomegranate-red colour, was saturated, one part with carbonic acid and another with oxygen; the oxygenous fluid exhibited no remarkable difference of colour from the original fluid, which was contained in a similar vessel; moreover, no distinct difference of colour could be perceived between the solution which was impregnated with carbonic acid and the normal fluid, or the solution impregnated with oxygen; but the solution of the blood-crystals through which carbonic acid had been passed was somewhat turbid and exhibited under the microscope large numbers of faintly granulated flakes. In vacuo the latter fluid developed a very large amount of gas, and

retained its turbidity and colour; these flakes remained unchanged when seen under the microscope. Both the normal fluid and the fluid impregnated with oxygen remained unchanged both as to colour and clearness in vacuo, although they developed relatively less gas. When the solution of blood-crystals was first saturated with oxygen, and then exposed to a stream of carbonic acid, the fluid became turbid without any marked changed of colour, and exhibited the same flakes under the microscope as the solution which had been treated directly with carbonic acid. If, however, a stream of oxygen be suffered to pass through the fluid, which has been rendered strongly turbid by carbonic acid, it at once becomes perfectly limpid without exhibiting any perceptibly increased lightness of colour. The substance may be again obtained in a crystallised form and unchanged, both from the turbid solution charged with carbonic acid and the clear fluid to which oxygen has been added. This separation of solid molecules by carbonic acid might seem to present a strong indication of a chemical action of the gases, but it could not be made to correspond with the opinion of Bruch,* that the normal colour of the substance in question is developed in the presence of carbonic acid. Other gases than oxygen and carbonic acid evidently exert a chemical action, like dilute organic acids, alkalies, &c.; this, for instance, is the case with carbonic oxide, for it not only very considerably darkens the deep red solution of the pure crystals, but it also gives rise to a dark brownish red coagulum (which exhibits great variety of form when seen under the microscope). Neither solutions of the original colour, nor crystals, can be procured from this fluid, either by repeated treatment with oxygen, or with carbonic acid and oxygen. Nitrous oxide renders the red fluid darker, almost brownish red, and very turbid, so that the microscope exhibits the whole fluid as if it were filled with flakes; neither oxygen nor carbonic acid restores the clearness or the original colour of the fluid, for the greater part of the substance crystallises unchanged. (Nitrous oxide may, therefore, be employed in the place of the oxygen in the mode of preparing the crystalline substance of the blood described at p. 491 of this volume, but it cannot take the place of the carbonic acid.) There can scarcely, therefore, be any doubt that the gases (oxygen and carbonic acid) exert a chemical action upon the colouring principle of the blood-corpuscles, as we see from these experiments, as well as from the entire mode of pre-

* Zeitsch. f. rat. Med. Bd. 1, S. 440-450, Bd. 3, S. 308-318, and Zeitsch. f. wissensch. Zoologie. Bd. 4, S. 373-376.

paration of the crystalline substance; although it would require far more extended investigations to exhibit the true mode of their operation. It would, however, be going too far, were we to conclude that the property which a protein-body exhibits of being modified in its character by oxygen and carbonic acid, is anything peculiar to this substance, or is any special attribute appertaining to this constituent of the blood-corpuscles. For, independently of the fact that, as we have already mentioned (see page 495 of this volume), globulin can be completely precipitated from its neutral solutions by carbonic acid, and the precipitate can be again dissolved by a stream of oxygen, certain modifications of the crystalline substance occur, which stand in precisely the reverse relation to these gases. I have described in p. 489 of this volume that modification of the crystalline substance which can be exhibited by acetic acid and an alkaline salt, and which corresponds with Panum's acid albumen (see page 478). When the faintly acid solution of this product of metamorphosis is carefully neutralised with a very dilute solution of potash, the substance will be perfectly precipitated; but this precipitate dissolves again in pure water, although not to any great extent, forming a pale red solution, from which the substance may be so completely thrown down by oxygen or by the action of the air, as only to leave a perfectly colourless fluid over the dirty flesh-coloured precipitate. On passing a stream of carbonic acid through this fluid, the precipitate redissolves into a pale red fluid. The substance may be again precipitated by oxygen, while the solution coagulates on boiling, in the same manner as albumen. These experiments, nothwithstanding their isolated character, contribute, together with what we have already stated in the last page, in reference to the influence of the gases upon the formation of the blood-crystals, to strengthen the probability that a chemical action may be impressed upon the main constituent of the blood-corpuscles by the alternating action of oxygen and carbonic acid, although opinions may differ as to whether this is manifested by an oxidation or a reduction, or whether it arise from the simple occurrence of carbonic acid as a conjugated acid, or finally, whether it be referrible to a salt-like compound.

Here I cannot refrain from observing that the substance corresponding to the acid albumen has not fallen under my notice as a product of decomposition of the true crystallisable matter of the blood, although Panum is of opinion that the albumen may be decomposed by acids and potash-salts into acid albumen and into

another organic substance. No other organic body is formed from the crystalline substance during the preparation of this matter; only a few phosphates separate from it, as is shown by my comparative analyses of the crystalline substance and of its products of metamorphosis, as well as by my investigation of the acid and saline fluid obtained after the removal of the precipitated bodies by filtration. It is only a metameric modification of the original crystalline substance.

I regret that Meckel's paper on hæmatoglobulin, contained in Scherer's Jahresbericht,* has only reached me while these sheets were passing through the press. According to Meckel, oxygen changes hæmatoglobulin to a bright red, and carbonic acid to a bluish red colour. It will be seen from my previous remarks, that I did not succeed with certainty in detecting this or any similar change of colour in the pure crystalline substance which I obtained. Moreover, according to Meckel, arterialised hæmatoglobulin is not crystallisable, and only the quantity corresponding to the globulin of venous blood (dem venosirten Globulin) crystallises from the blood,—a fact which it seems to me difficult to prove, as Meckel appears entirely to have overlooked the influence of light upon the formation of the crystals. Although it may be *à priori* highly probable that hæmatochlorin and hæmatoïdin *appear* to be produced from hæmatoglobulin by oxidation, I cannot discover any chemical proof of the fact in Scherer's report. Meckel also employed a stream of carbonic acid in the crystallisation of his hæmatoglobulin, and in the course of his experiments he made numerous valuable observations, which tend to confirm many otheir researches, more especially those of Kunde and Funke.

(22) Addition to p. 208, line 6.—It appears from the investigations of Guillot and Leblanc,† Panum,‡ Stas,§ and others, that the substance which they regard as *casein*, is contained in a larger quantity in the blood of pregnant and puerperal women than in ordinary blood. The supposed occurrence of casein in the blood has been already noticed in page 483 of this volume.

Notwithstanding the proofs which Panum and Moleschott have brought forward to demonstrate the existence of casein in the blood, Scherer is still by no means convinced that their casein

* Jahresber. d. ges. Med. 1852, S. 95.

† Compt. rend. T. 31, p. 585.

‡ Arch. f. path. Anat. Bd. 3, S. 268.

§ Compt. rend. T. 31, p. 629.

is anything more than albuminate of potash or soda. See vol. i, p. 334.

(23) Addition to p. 224, 15 lines from the bottom.—Vierordt,* has recently succeeded, by means of very comprehensive and unusually laborious investigations, in sketching a method of a blood-analysis, which promises to supply some of those deficiencies in Schmidt's method, which have been felt by all experimentalists, and may therefore serve in some degree at least as a check upon the latter. If we were able to determine the numerical quantity and the volume of the blood-corpuscles in every kind of blood to be analysed, we should naturally have no difficulty in obtaining their relations of weight in the blood, and of determining by a simple calculation from the further analysis of the blood the amount of constituents appertaining to the blood-corpuscles. Vierordt was thus led, at the expense of much time and labour, to calculate the number of the blood-corpuscles in the two following ways. In the one method, a small volume of unmixed blood was measured in a capillary tube, and then introduced into what he termed a diluting fluid (a tolerably concentrated solution of albumen or gum), with which it was spread out under the microscope, and the corpuscles were then counted by means of two glass micrometers, which had been graduated expressly for this purpose, and were respectively attached to the eye-piece and the object-glass. By the other method, an accurately measured volume of blood was mixed with an equally accurately measured volume of diluting fluid, and a microscopic volume of this mixture was employed for the counting of the corpuscles. Welker† has recently suggested certain modifications in Vierordt's method.

Vierordt does not determine the volume of the blood-corpuscles by direct measurements, but by a simple calculation, which is perhaps scarcely exact enough. This calculation, as well as that of the whole blood-analysis, depends essentially upon the circumstance that comparative analyses are made of the whipped blood, rich and poor in corpuscles; according to Vierordt, the blood is rendered poor in corpuscles either by the filtration of the whipped blood through paper, or by the addition of a definite quantity of previously analysed serum. All persons familiar with the principles of mathematics will readily comprehend Vierordt's ingenious method, although they must at the same time perceive that, for

* Arch. f. physiol. Heilk. Bd. 11, S. 26-73, 327-332, 547-558, and 854-884.

† Fechner's Centralbl. 1853. No. 12, S. 218-222.

these calculations, besides the exact counting of the corpuscles in each analysis, it is necessary to assume one, if not two, probable magnitudes.

If we abstain from entering more fully into this subject, and for the present withhold our judgment on a question of physiological chemistry which promises to be of the highest importance to physiology generally, this does not arise from a want of appreciation of the great merits of Vierordt in this department of chemistry, but simply because we do not regard a manual of this kind as a suitable place for the introduction of investigations of this nature, and because we have been anxious, as far as possible, to base our judgment solely upon our own experiments and upon *post mortem* examinations. In consequence of the different direction of our own investigations regarding the blood, we are hardly in a position to criticise in their individual details the labours of Vierordt. Such a critical and experimental testing is, however, indispensably necessary before we can form a correct judgment of this method, as a number of considerations force themselves upon our notice, which, although they have in part been explained by Vierordt himself, are still sufficiently numerous to demand an experimental examination. O. Funke,* among others, has shown with much clearness the possible causes of error which appertain to this method. For the present, we may regard Schmidt's method of blood-analysis, of which we have considerable experimental knowledge, as the one which, notwithstanding some well-known deficiencies, affords the most certain results.

(24) Addition to p. 227, line 19.—Vierordt † found in his various countings that in 1 cubic millimetre [the linear millimetre being about 1-25th of an inch] of normal blood obtained by pricking the finger, there are on an average 5,055,000 blood-corpuscles; Welker,‡ on the other hand, fixes the number at 4,600,000.

(25) Note to p. 237, 7 lines from the bottom.—[The view stated in the text, that the colourless were to the red corpuscles in the ratio of 1 : 8 or 1 : 10, is now exploded; Henle makes the ratio as 1 : 80; Donders and Moleschott subsequently showed that 1 : 373 was about the average ratio. Moleschott§ has re-

* Schmidt's Jahrb. d. ges. Med. Bd. 74, S. 1-7, and Bd. 78, S. 5-9.

† Arch. f. physiol. Heilk. Bd. 11, S. 867-874.

‡ Fechner's Centrabl. 1853. No. 12, S. 22?.

§ Wien. med. Wochenschr. No. 8. 1854.

cently experimented upon seven individuals of different ages, with the following results. The numbers are in every case the mean of several countings.

In children from $2\frac{1}{2}$ to 12 years	1 : 226
In young men from 21 to 22 years	1 : 330
In men „ 30 to 50 „	1 : 346
In old persons „ 60 to 80 „	1 : 381
In young women from 14 to 38 years, when not menstruating	1 : 389
In young women when menstruating....	1 : 247
In „ when pregnant	1 : 281

The view formerly held by Donders and Moleschott, that the colourless corpuscles increase shortly after taking food, and diminish on fasting, is confirmed by more recent observations independently made by Moleschott, who especially finds that food rich in albumen increases their number much more considerably than food poor in that substance.—G. E. D.]

(26) Addition to p. 238, line 9.—It is principally in the disease first recognised by Virchow, and named *leucæmia* by him [and independently discovered by Bennett, who terms it *leucocythæmia*], that we find a very great augmentation of the colourless corpuscles, their ratio to the coloured ones being often as 1 : 3; they consequently communicate a pale red colour to the blood.

Moreover, the blood of the splenic vein is richer in colourless cells of various forms than that of any other vessel, as has been especially shown by Funke.* It has been already mentioned (vol. ii, p. 106) that I found the blood of the hepatic veins much richer in colourless cells than that of the portal vein.

(27) Addition to p. 239, line 10.—We have already spoken, in vol. i, p. 358, of the different amount of fibrin contained in the blood in diseases. It appears, from the most recent analyses of Becquerel and Rodier,† that the amount of fibrin may vary very considerably in the same group of diseases, in one case rising above and in another falling below the mean number; as, for instance, in dropsies, and in the most various forms of heart-disease; in chlorosis the quantity of fibrin is either normal, or amounts to 0·1 or 0·2% above the normal quantity; the reverse is

* Diss. inaug. Lips. 1850; and Zeitschr. f. rat. Med. N. F. Bd. 1, S. 172-218.

† Gaz. méd. de Paris. 1852. No. 24, 25, 26, 30, 31.

the case in anæmic conditions, in which we frequently observe a diminution of this constituent. While no increase of the fibrin was observable in the acute form of Bright's disease, chronic cases of that disease presented an almost constant augmentation of this constituent.

In scurvy Becquerel and Rodier found a constant diminution of the fibrin, but unfortunately these writers have designated as scorbutic that condition in which, in consequence of other grave diseases, the fibrin of the blood falls below 0·2%; on the other hand, in acute idiopathic scurvy, there was rather an augmentation of the fibrin. As long as such a want of clearness appertains to our ideas of certain diseases, and their various characteristics are so unsystematically confounded, pathological chemistry can make no positive advance, notwithstanding all the efforts devoted to the study of this branch of science. It seems to us that Becquerel and Rodier would have done far more to advance pathology if they had investigated the excretions and some of the secretions conjointly with their analysis of the blood in any single patient, instead of making numerous and laborious determinations of the blood in similarly named but not analogous morbid conditions.

(28) Addition to p. 253, line 8.—This is the more striking as von Becker* has found, from numerous and variously modified experiments which he instituted in my laboratory, that, at all events in rabbits, sugar cannot be detected in the urine, unless the blood contains as much as 0·5% of that substance. Von Becker has moreover very distinctly shown, by direct experiments, that highly saccharine food exerts an influence on the amount of sugar in the blood. Thus, for instance, he found that the blood of rabbits which had been solely fed on carrots yielded 0·584% of sugar, whilst there was only 0·109% in the blood of those animals when fed upon oats, and only 0·045% in their blood when they had fasted 24 hours. As much as 1·198% of sugar was found in the blood of a rabbit which had been so abundantly supplied with sugar from time to time during several hours, that some of this substance had even passed into the solid excrements.

It was the more important to show, by direct experiments, that food exerted a decided influence on the amount of sugar in the blood, since O. Funke, Bernard, and myself had failed in detecting sugar in the portal blood. Notwithstanding its impro-

* Zeitschr. f. wissensch. Zoologie. 1853. Bd. 5, S. 123.

bability, the idea readily suggested itself that all the sugar which was found in the blood originated solely in the liver; and that that which was formed during digestion was further metamorphosed in the intestinal canal. [This subject is further noticed in pp. 276–291 of the present volume.] Moreover we learn from a careful clinical observation, that, at all events in diabetic patients, a saccharine food exhibits an influence on the amount of sugar in the urine.

There is considerable difficulty in determining the greatest quantity of sugar which can exist in the blood without inducing saccharine urine, and this difficulty may, perhaps, account for the small quantity of sugar found by myself in the blood of a diabetic patient, when compared with that which was found by von Becker in rabbits in which artificial diabetes had been induced by pricking the floor of the fourth ventricle, and in other rabbits, whose blood had been rich in sugar: hitherto von Becker has found that where the blood contains 0·4% of sugar, no portion of it passes unchanged into the urine, although a decided sugar-reaction might be detected in the urine obtained by pressure on the region of the bladder, when its quantity in the blood amounts to 0·6% of this substance. The difference in the nature of the urine in man and these animals may perhaps explain the cause of the high amount of sugar which must be present in the blood of rabbits before it appears in their urine, whilst I could discover so little sugar in the blood of diabetic patients; the alkaline urine of rabbits, as we learn from direct experiments externally to the organism, metamorphoses sugar far more rapidly into acid than human urine; we must, moreover, bear in mind that diabetic urine is so poor in matters exciting fermentation, that it passes very slowly into a state of fermentation, which may perhaps in some measure explain the difference. I* have, moreover, long since shown that freshly passed urine does not react on vegetable colours in cases of well-marked diabetes, that it is deficient in several of the ordinary extractive matters of normal urine, and that it only gradually acquires an acid reaction on standing exposed to the open air.

(29) Addition to p. 257, line 20.—Genth† has also recently examined the ash of the blood of Limulus Cyclops, which, when fresh, has an azure blue colour, and has found in it a considerable quantity of copper with a little iron. In two analyses of the ash of this blood, he found in 100 parts:

* De urina diabetica. Diss. inaug. Lips. 1835.

† Keller u. Tiedemann's Nordam. Monatsschr. Bd. 3, S. 438-441.

Oxide of copper, with traces of oxide of iron	0·297	0·083
Chloride of sodium	72·907	83·507
Phosphoric acid	0·683	0·281

The blood had a specific gravity of 1·0317 and yielded 3·327% of ash.

(30 Addition to p. 260, 12 lines from the bottom.—Funke's very carefully conducted examination of the blood of the splenic vein in horses does not, unfortunately, either confirm or refute Béclard's conclusions, while my own experiments on the arterial blood of the same animals (from which the blood of the splenic vein had been taken) exhibited such different results, that no general deductions could be obtained in reference to any one point. The juice expressed from the spleen which J. Scherer* analysed consisted principally of blood, yielded by the capillaries of the spleen. Scherer found that it contained in addition to albuminous matters and salts, lienine, hypoxanthine, two different kinds of ferruginous pigments, a large amount of free iron not combined with pigments, and acetic, formic, and lactic acids.

This investigation of Funke affords, at all events, a proof that the greatest caution is necessary in deducing conclusions from individual analyses and investigations of individual fluids, without reference to the simultaneous constitution of the other animal juices. Many ingenious conclusions would no doubt have been deduced from analyses of the blood of the splenic vein, if the arterial blood had not been simultaneously compared with it.

(31) Addition to p. 261, line 8.—The blood of the *placental vessels* contains, according to Stas,† little albumen and fibrin, whose place is, however, supplied by a large amount of a substance which he calls casein (see p. 483 of this volume). Stas also believes that he has found urea in this blood.

(32) Addition to p. 261, 14 lines from the bottom.—C. Schmidt‡ has endeavoured by careful and numerous experiments to establish the proposition, that *the loss of albumen in the blood is supplied by a relatively corresponding amount of salts*, as for instance, *chloride of sodium.* Thus we find that wherever albumen is lost from the blood, either by accidental or intentional blood-letting, by morbid exudation from the capillaries of the

* Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 323.

† Compt. rend. T. 31, p. 630.

‡ Charakteristik der Cholera, S. 69.

serous membranes (dropsy), by the action of the kidneys (albuminuria), or by other losses of the juices whose action is manifested by a diminution of albumen in the blood, certain quantities of the albumen lost from the blood are replaced by certain quantities of soluble salts, and here we must bear in mind that the salts are in general accompanied by a definite quantity of water, which differs from the amount associated with the albumen. The experiments of Kierulf * have recently furnished a new proof of the correctness of these observations, for he found that after a considerable quantity of water had been injected into the veins, the amount of the salts in the blood was rapidly and permanently increased.

(33) Addition to p. 266, 11 lines from the bottom.—In *leucæmia*, which is commonly associated with a considerable enlargement of the spleen, the entire mass of the blood exhibits considerable similarity with the blood of the splenic vein (Virchow, Scherer). The blood from the most different vessels is pale red, often marked with whitish streaks and very rich in colourless blood-corpuscles; within the body it coagulates into gelatinous flakes, but when it coagulates in the air very little serum separates from it; it exhibits an alkaline reaction, although the fluid which is filtered from the coagulum has an acid reaction; according to Scherer's investigation, this blood contains true glutin, also a body which ranks between glutin and albumen (an albuminous substance containing phosphorus and iron), hypoxanthine, and finally formic, acetic, and lactic acids. In other respects, according to Scherer's analysis,† its quantitative composition is nearly the same as that of normal blood in respect to the main constituents, excepting that the iron seems to be present in a somewhat smaller quantity.

(34) Addition to p. 266, 4 lines from the bottom.—Becquerel and Rodier have been led by their most recent analyses, which, however, are not very conclusive, to adopt the opinion that "the essential anatomical character of scurvy must be sought in an original modification of the fibrin," while they show that there is an increase of the fibrin in the acute form of the idiopathic disease, ' depending upon an excess of the soda-salts in the blood."

(35) Addition to p. 270, line 11.—The following method, based

* Mitth. d. naturf. Ges. z. Zürich. Juli 1852.

† Verh. d. physik-medic. Ges. zu Würzburg. Bd. 2, S. 321-325.

upon the amount of sugar contained in the blood, will, I believe, afford an average estimate of the quantity of blood in animals: if we know how much sugar the blood may under the most favourable conditions contain, without its appearing in the urine, and if we determine how much sugar the blood may normally contain on an ordinary diet, we may be able to calculate the quantity of blood contained in an animal by ascertaining the quantity of sugar which must be introduced by injection into the jugular veins, or by some other method, in order to make it pass into the urine. We know from von Becker's investigations (see p. 529 of this volume) that about 0·5% of sugar may exist in the blood without passing into the urine, and that further, after the use of saccharine roots the blood contains 0·67% of sugar. Now I find from my own, as well as from Uhle and von Becker's injections of sugar (grape-sugar), that when 0·2 of a gramme of sugar was injected into the blood of rabbits of the ordinary size (1200 grammes' weight), the urine indicated the presence of sugar in 25 minutes. If now we assume that in a rabbit weighing 1 kilogramme, 0·15 of a gramme of sugar injected into the blood will saturate it to such an extent, that if there were any additional quantity of sugar it would appear in the urine, a rabbit of this weight will contain 95·8 grammes of blood. Dr. von Becker is still engaged on experiments of this kind. In the present uncertainty of all the methods for determining the amount of blood in the animal body, a method like the above should not be wholly overlooked, although it may not present any great guarantee for its accuracy; since the agreement of the results of different methods would increase the degree of probability for the determination of the definite amount of blood contained in individual organisms.

(36) Addition to p. 303, line 18.—Bidder* believes, from his experiments on animals, that in an adult man about 13 kilogrammes [about 28·6 lbs.] pass in the course of 24 hours from the thoracic duct into the subclavian vein. He is of opinion that only 3 kilogrammes [6·6 lbs.] are true chyle (or digested nutrient matter), and that 10 kilogrammes [22 lbs.] are true lymph. Hence in the course of 24 hours a quantity of lymph, averaging from 1-8th to 1-7th of the weight of the body is formed and poured into the blood.

* Verdauungssäfte und S offwechsel. S. 285.

(37) Addition to p. 335, line 20.—Knobloch* instituted a series of experiments upon one and the same cow in reference to the constitution of the milk at different seasons of the year, and according to the length of time during which each milking was continued. From these observations it would appear in reference to the amount of casein in the milk, in the first place, that its quantity is greater towards the close than at the beginning of each individual act of milking, whilst the quantity of water decreases; and in the second place, that the milk is poorer in casein on winter than on summer fodder. In winter the amount of casein and of salts insoluble in spirit rose during the milking from 7·07% to 7·08%, whilst in summer it varied from 8·40% to 8·67%.

(38) Addition to the bottom of p. 339.—Moleschott† found that the milk of two cows had a strongly acid reaction several days before and after calving during the winter.

(39) Addition to p. 347, 15 lines from the bottom.—Dr. von Becker recently made several observations in my laboratory, which afforded the first experimental proof of a fact which had been long assumed. In his experiments on the resorption of sugar, he found, that in order to make sugar appear in the urine of rabbits, whose udders contained milk, it was necessary to introduce a much larger amount of that substance into the blood than in the case of male or non-suckling rabbits. In these cases there was also far less sugar in the blood than a comparison with other experiments would have led us to anticipate. The grape-sugar introduced into the blood, must, moreover, have been very rapidly absorbed by the mammary glands in these cases.

(40) Addition to p. 355, line 23.—The ova of amphibia and fishes contain the so-called *yolk-plates*, or tablets, which have in part square, and in part other crystalline forms, and very frequently present a distinctly stratified appearance. Histologists (Bergmann) have long been acquainted with these bodies, and have usually regarded them as fat (stearin). Virchow§ has recently submitted them to a more exact micro-chemical examination, and has shown

* Kunst und Gewerbeblatt f. d. k. Bayern 1851, S. 144-147.
† Arch. f. physiol. Heilk. Bd. 11, S. 696-698.
‡ Müller's Arch. 1841, S. 89.
§ Zeitschr. f. wissensch. Zool. Bd. 4, S. 236-241.

that they cannot belong to any of the known fats, but very probably constitute a new substance, which has considerable similarity to the protein-bodies, especially in their relation towards nitric acid and Millon's reagent. According to Virchow these plates remain undissolved in ether and boiling alcohol, although they swell in both fluids, become pale, and sometimes burst into several pieces; the same observer found that they behaved in a similar manner towards acetic acid, dilute mineral acids and alkalies, chloroform, glycerine, &c. The square tablets thus become oblong, or often oval. They dissolve in concentrated acetic acid and caustic alkalies, merely leaving small membranous particles or larger pale flakes.

(41) Note to pp. 385–393, on the Sweat.—[Favre,* who asserts that he has operated on 40 litres (or 8·8 gallons) of sweat, maintains, that after prolonged sweating the secretion becomes neutral, and finally alkaline; Lehmann, however, was unable to confirm this observation; it is to be regretted that Favre has not stated how he collected this enormous quantity.

The solid constituents amount, according to Schottin,† to 2·26%, while according to Favre they do not exceed 0·443%. In these 2·26% of the solid constituents of normal sweat, Schottin found 0·42% of epithelium and insoluble matters. In 100 parts of the ash of the sweat he found 31·3 parts of chlorine, combined with 28·2 of sodium and 11·1 of potassium; the ratio of the potassium to the sodium in the ash was as 15·7 : 27·5.

In the ash of the sweat from the feet he found 4·1% of phosphate of lime, and 1·4% of phosphate of magnesia and oxide of iron. Moreover, in two closely coinciding analyses of the ash of sweat from the feet and arms, he found 5·5% of insoluble and 94·5% of soluble mineral constituents.

The organic acids of the sweat were never strictly investigated until Schottin undertook the examination of this fluid: he has demonstrated with the greatest certainty the presence of *formic* and *acetic acids* in it. Lehmann considers it singular that the formic acid should preponderate so much, as seems to be the case, over the other volatile acids; the acetic acid was in far smaller quantity, and butyric acid was present in new traces.

For a long time the presence of *lactic* acid in the sweat was regarded as an accepted fact; but Lehmann failed in detecting

* Compt. rend. T. 35, p. 721-723; and Arch. gén. de Méd. 1853, 5e Sér. T. 2, pp. 1-21.

† Arch. f. physiol. Heilk. Bd. 11, S. 73-104.

any trace of it in the sweat either of puerperal women or of persons suffering from gout or rheumatism, and it was unquestionably proved that this acid was not present in the sweat collected by Schottin. Favre, who seems to have entirely overlooked the presence of volatile acids in the sweat, maintains, however, that he has not only demonstrated the existence of this acid by the exhibition of its zinc-salt and elementary analysis, but that he has determined the actual quantity of the lactate of potash and soda in the sweat at 0·0317%.

Favre further believes that he has discovered a new nitrogenous acid in the sweat, to which he has given the name of *hydrotic* or *sudoric acid.* From two elementary analyses of its silver-salt he assigns to it the formula $C_{10} H_8 NO_{13}$.

With regard to the presence of *urea* in the sweat, Favre regards it as a normal constituent, and he thinks that it is upon its presence or that of a similar substance that the readiness with which the fluid becomes alkaline depends; but notwithstanding the most careful search, Schottin failed in detecting it, either in the normal sweat generally, or in the sweat of the feet which so soon becomes alkaline. Schottin, however, made the interesting observation (see foot-note to vol. ii, p. 388) that in *uræmia* (especially when occurring in cases of cholera) considerable quantities of urea pass into the sweat.

We sometimes find the bodies of persons who have died from cholera coated with a thin bluish layer, which on closer examination is found to consist of a fine powder, composed, for the most part, of urea.

Lehmann was unable to detect any trace of *sugar* in the sweat of a diabetic patient, who, contrary to the general rule, perspired very copiously in a hot summer.

Schottin has instituted several very admirable experiments on *the passage of several matters into the sweat,* and from these it would appear that *benzoic acid,* and also succinic and tartaric acids, pass very rapidly and unchanged into the sweat. Iodide of potassium was not detected in the sweat until it had been taken for five days (half a drachm daily). When salicin was taken, neither this substance itself nor any of its known products of decomposition, could be detected in the sweat. Quinine, taken to the amount of 12 grammes, did not pass into the sweat. After the ingestion of much *sugar of milk,* neither a saccharine matter nor lactic acid appeared in the sweat.

It would be very interesting to decide, whether the benzoic

acid found by Schottin in the sweat is produced from the decomposition of hippuric acid by the sweat, or whether the acid is separated unchanged by the sweat-glands without being previously converted into hippuric acid (as when it is separated by the urine). As cinnamic acid would appear from the discovery of Marchand and Erdmann to be separated by the kidneys as hippuric acid, this question might apparently be determined by an examination of the acid that appears in the sweat after the use of cinnamic acid; for if, instead of the latter, benzoic acid should appear, it would tend in some degree to favour the opinion that the cinnamic acid was first converted into hippuric acid, from which the benzoic acid was then produced. If, on the other hand, cinnamic acid were found in the sweat, it would afford greater probability to the view, that the benzoic acid found in the sweat could not have been converted into hippuric acid before its excretion. Unfortunately, however, the quantity found in Schottin's experiments was no more than sufficient for a microscopico-chemical examination, but the microscope could not settle this point definitely, owing to the great resemblance between the crystalline form of these two free acids and of their salts.—G. E. D.]

(42) Addition to p. 400, line 2.—We must, however, observe that the extractive matters occur in very variable quantities in the urine, more especially during disease, although it may also be the case in health during different physiological relations. Thus, for instance, Scherer* found that children, in relation to their bodily weight, excrete far more extractive matter through the urine in 24 hours than adults. He found that the sum of the excretion was 0·346 of a gramme in the 24 hours for every kilogramme's weight of a child, while in the case of an adult it was only 0·156 of a gramme for every kilogramme's weight. Scherer, moreover, made a very remarkable observation on an insane person, who, although he had scarcely taken any nourishment for four weeks, yet discharged a large quantity of extractive matters, exceeding even the amount of the urea; thus, for instance, he excreted 9·48 grammes of urea and 10·59 grammes of extractive matters in the 24 hours.

(43) Addition to p. 400, 2 lines from the bottom.—Hegar†

* Verhandl. d. phys.-med. Ges zu Würzburg. Bd. 3, S. 187-190.

† Ueber die Ausscheidung der Chlorverbindungen durch den Harn. Inauguralabh. d. med. Fac. zu Giessen vorgel. 1852.

has recently instituted experiments, under the direction of Julius Vogel, on eight persons, for the purpose of ascertaining the fluctuations in the amount of chlorine in the urine: the following are the results of these investigations; the mean amount of chlorine in the urine is 10·46 grammes in the 24 hours, although the quantity varies very considerably in different persons. In the afternoon the secretion of chlorine is at the maximum (although not immediately after dinner), in the night it sinks the lowest, and again rises in the morning. Bodily exertion increases the excretion of chlorine; indisposition diminishes it somewhat rapidly. The secretion is augmented by drinking water, but it is afterwards proportionally diminished. When chlorine-compounds are taken after fasting, the secretion remains for some time less than it would otherwise have been. Even when no chlorine-compounds are introduced into the system from without, a little alkaline chloride is still separated with the urine. When more than the usual amount of chlorine is taken up, the secretion is simply augmented for a short time; but, on the whole, less chlorine is excreted by the urine than is taken up; the excess of chlorine must, therefore, be eliminated by some other channel.

(44) Addition to p. 401, line 14.—Redtenbacher* has, however, seen in 80 cases of pneumonia that the amount of the chloride of sodium fell to a minimum; at the crisis of the disease nitrate of silver actually yields no precipitate in acidified urine; with the decrease of the inflammatory process the chlorides again gradually increase. Even after the use of hydrochloric acid, Redtenbacher was unable to detect any chlorine in the urine of persons affected with pneumonia. According to the same observer, the chlorine disappears for a short time from the urine during relapses in pulmonary tuberculosis. In acute rheumatism, capillary bronchitis, and typhus, the chlorine frequently, although not constantly, disappears from the urine for a short time.

We have already spoken in vol. i, p. 446, of the amount of sulphates present in normal urine. Observations have been instituted in reference to the fluctuations occurring in the amount of sulphuric acid present in the urine; among these analyses, those of Bence Jones† and of Gruner,‡ conducted under the direc-

* Ber. d. kais. Ak. d. Wiss. zu Wien. 1850.

† Philosophical Transactions. 1849, pp. 252-260.

‡ Die Ausscheidung der Schwefelsäure durch den Harn. Inaug.-Abh. der med. Fac. zu Giessen vorgel. 1852.

tion of Julius Vogel, deserve special notice; the following were the results which were obtained: an adult (whose bodily weight is 60 kilogrammes) discharges on an average 2·094 grammes of sulphuric acid in 24 hours (Gruner). The amount of excreted sulphuric acid rises during the period of digestion, falls somewhat in the night, and is at its minimum in the forenoon (Gruner and Jones). Active bodily exercise and mental excitement seem alone able to influence the increased secretion of sulphuric acid in the urine; moderate exercise does not influence it (Jones and Gruner). Fasting does not diminish the excretion of sulphuric acid, at least during the first 24 hours. This secretion is increased for a short time, but afterwards proportionally diminished, by copious draughts of water (Gruner). Sulphate of soda, potash or magnesia, is perfectly eliminated by the urine in 18 or 24 hours after it has been taken (Gruner and Jones). The amount of sulphuric acid in the urine also increases after the administration of sulphur.

(45). Addition to p. 402, line 19.—Careful investigations have been instituted by Breed* and by A. Winter,† in reference to the amount of phosphoric acid in the urine. The mean of several experiments on different individuals showed that there were eliminated in the 24 hours from 3·765 to 5·180 grammes (Winter), or 3·732 grammes (Breed). An increased use of fluids slightly raises the number of the excreted phosphoric acid (Breed), but according to Winter this is only observable in the first three or four hours. In the night very much more phosphoric acid is eliminated than in the morning, although then even less than at noon (Winter). The amount of excreted phosphoric acid rises very considerably after taking food (Breed and Winter).

(46) Addition to p. 404, line 10.—Falk ‡ has instituted very careful investigations in reference to the same subject, and has obtained very opposite results; but three experiments are not sufficient to warrant us in regarding this question as finally settled. According to Falk's observations, water is eliminated in about six hours after it has been taken, while a certain quantity of urine is eliminated in a fasting state, even when no water has been introduced into the organism.

* Ann. d. Ch. u. Pharm. Bd. 78, S. 150-152.

† Beiträge zur Kenntniss der Urinabsonderung bei Gesunden. Inauguralabh. d. med. Fac. zu Giessen vorgel. 1852.

‡ Arch. f. physiol. Heilk. Bd. 12, S. 150-155.

(47) Addition to 404, line 19.—Some interesting experiments on the influence of the injection of water into the blood simultaneously with blood-letting, have been made by Kierulf,* in Ludwig's laboratory. It would appear from these observations, that a considerable attenuation of the blood generally gives rise to a secretion of albumen through the kidneys, followed by hæmaturia, which, however, is probably not accompanied by laceration of the capillaries of the kidneys. The rapidity with which the urine was secreted bore no proportional relation to the amount of water contained in the blood.

(48) Addition to p. 406, line 17.—The fluctuations in the amount of free acid in the urine during health have been made a special object of attention by Bence Jones† and A. Winter.‡ A. Winter found that an adult of average bodily weight (67 kilogrammes) discharged in the 24 hours as much free acid as would correspond with 2·304 grammes of oxalic acid. (The amount of the free acid was determined by means of a solution of ammonia of known strength.) It appeared, moreover, from the experiments of both these observers, that during the period of digestion, that is to say, in the afternoon hours, the quantity of the free acid was at its mean; it attained its maximum during the night, and fell far below the mean during the forenoon. It would appear from the experiments of Jones, that the diminution of the free acid was more decided after the use of animal food than after the use of mixed food, and more especially of a vegetable diet, which is the more remarkable, since we know that a purely vegetable diet gives a very faint acid or even an alkaline reaction to the urine, whilst the latter becomes very acid after the use of animal food (see my investigations on the urine under different modes of diet), this being the case, as Bernard has observed, even in herbivorous animals, which usually discharge an alkaline urine. Nevertheless, these observations, which are in direct opposition to our own experiments, deserve to be more carefully investigated.

(49) Addition to p. 415, 14 lines from the bottom.—The ammonia of the *ammoniacal salts* passes for the most part unchanged into the urine.

* Mitth. der naturf. Ges. zu Zurich. Juli 1852.

† Philosophical Transactions. 1849, pp. 235-251.

‡ Op. cit.

Bence Jones* believes that he has convinced himself, by numerous experiments, that after the use of ammoniacal salts (he employed the carbonate, tartrate, and hydrochlorate of ammonia), nitric acid might always be detected in the urine, and consequently that the power of oxidation possessed by the organism is so great, that the nitrogen of the ammonia is oxidised into nitric acid. I regret that this observation must be regarded as so far erroneous, that the method employed by Jones for the discovery of nitric acid must necessarily yield a reaction which is similar to that of nitric acid. Jones decomposed about four ounces of urine with half an ounce of concentrated sulphuric acid, and distilled two-thirds of the fluid in a retort; in the fluid thus yielded by distillation, Jones thought he might determine the amount of nitric or nitrous acid by Price's method (which is a mixture of starch, iodide of potassium, and hydrochloric acid). In some experiments which I made, I certainly found that the distilled fluid, when treated with iodide of potassium and hydrochloric acid, turned starch blue. In the meanwhile it would seem chemically incomprehensible how nitric acid, if it really were present in the urine, could pass unchanged from it during its distillation with sulphuric acid; we need only observe that in this concentration of the fluid, the chloride of sodium, as well as the supposed nitrate in the urine, will be decomposed by the sulphuric acid, and that nitrous acid must be formed together with free chlorine, but the former is at once decomposed into nitrogen and water, on being brought in contact with urea; the undecomposed nitric acid, if any could be present, would also be decomposed on boiling. Now it is easy to see that sulphurous acid, by which, as is well known, hydriodic acid is decomposed, passes into the receiver, and thus probably induces this supposed nitric-acid reaction. The following results were obtained from the experiments which were made in my laboratory by Jaffé, one of my students, for the purpose of verifying this proposition: ordinary urine, when no ammoniacal salts had been taken, was found to yield this reaction when treated by Bence Jones's method; this reaction, however, did not occur when the distillate had stood for some time in the air, in which case the sulphurous acid had become converted into sulphuric acid. The distillate, even after the most careful distillation with sulphuric acid, always yielded, with chloride of barium, a precipitate which was insoluble in acids and much water, but this precipitate is not formed when the urine has been treated with phosphoric instead

* Philosophical Transactions. 1851, pp. 399-409.

of sulphuric acid, and then distilled. The distillate which was obtained after the application of phosphoric acid, does not exhibit this supposed nitric-acid reaction even when the urine has been previously treated with some drops of nitric acid. Jaffé modified this experiment in various ways, but the methods we have already given are sufficient to show that the presence of nitric acid in the urine cannot be proved by Jones's method, even when it occurs in moderate quantities, and that Price's method for detecting nitric acid is altogether inapplicable when sulphurous acid is present. We must therefore, for the present, leave the somewhat improbable view of the conversion within the organism, of ammoniacal salts into nitric acid, as a subject requiring further investigation before it can be regarded as settled.

[Dr. Bence Jones* has defended his former views in a memoir recently read (June 15, 1854) before the Royal Society, "On the oxidation of ammonia in the human body." In this paper he describes a series of experiments, from which it results:—

1st. That in Price's test sulphurous acid produces exactly the opposite effect to nitrous acid, and even hinders nitrous acid from liberating iodine from hydriodic acid.

2nd. That phosphoric acid, when mixed with urine containing nitre, and distilled very low, does liberate nitrous acid; though when used instead of sulphuric acid, it does not enable the nitrous acid to be detected so readily as when the latter acid is employed.

"Hence (he observes) the experiments performed in Professor Lehmann's laboratory by Herr Jaffé†, do not invalidate Price's test for nitrous acid in the way Professor Lehmann supposes; and by again repeating some of my former experiments, I still arrive at the conclusion that when ammonia is taken into the body, nitric acid may be detected in the urine, but that the quantity which can be made to appear is so small that the most delicate method is required for its detection. This, however, is no proof that a much larger quantity may not be lost in the process for obtaining it from the urine."—G. E. D.]

(50) Addition to p. 420, line 21.—Ranke‡ found that after the use of *amygdalin* considerable quantities of formic acid passed into the urine, an observation which I thoroughly confirmed in my experiments on the injection of amygdalin into the veins.

* Proceedings of the Royal Society. Vol. 7, p. 94.

† Journ. f. pr. Chem. Bd. 59, S. 238.

‡ Ibid. Bd. 56, S. 17.

The action of amygdalin, when injected into the blood, is therefore never injurious, since no prussic acid is formed.

Salicin generally undergoes a change corresponding to oxidation in the organism; and it is only when taken in very large quantity that a portion of it passes undecomposed into the urine. The experiments instituted by myself as well as by Ranke* on the metamorphosis of salicin, give the following results: after the introduction of salicin into the body by the mouth, we find in the urine not only salicylous and salicylic acids, but also saligenin, while no sugar and no phenylic acid can be detected (see p. 238 of this volume). The salicin must be for the most part decomposed in the blood, for whenever I have injected a solution of this substance into the jugular vein in rabbits, substances were found in the alcohol-extract of the urine which yielded, with the persalts of iron, the blue colour corresponding to saligenin and salicylous and salicylic acids.

(51) Addition to p. 422, line 3.—I have recently observed in the same individual that the urine was expelled in nearly alternating jets from the two ureters four minutes after he had taken half an ounce of acetate of potash, while the urine became alkaline in the course of seven minutes. In the meanwhile it ought to be observed that the constitution of the individual probably exerts some influence on the rapidity with which such substances are transmitted into the urine, and that in this patient the rapidity may have been unusually great. I certainly have never found, in any of the numerous experiments conducted in my laboratory, that such substances as iodine, ferrocyanide of potassium, and alkaline carbonates, passed so rapidly into the urine as in either the older or more recent observations made on this person.

(52) Addition to p. 426, 12 lines from the bottom.—Fat, however, sometimes occurs in perfectly normal urine. I found that it was constantly present, although in small amount in the urine of tortoises (*T. græca*); Frerichs† commonly found it in the urine of cats, and the subsequent carefully conducted investigations of Lang‡ confirmed this observation. The latter observer also detected a small amount of fat in human urine, especially after the

* Journ. f. pr. Chem. Bd. 56, p. 1-11.

† Die Bright'sche Nierenkrankheit. u. deren Behandl. Braunschw. 1851, S. 154.

‡ De adipe in urina et renibus diss. inaug. Dorp. Liv. 1852, pp. 6-46.

use of fatty food; and the various experiments which were made by him on cats, as well as on men, leave no doubt that the occurrence of fat in the urine is frequently to be referred to the food. Whether, however, this is the sole cause of the occasional appearance of fat in the urine of healthy animals, appears from the observations which I have made on the urine of tortoises and on the kidneys of the deer (see p. 465 of this volume), to be a matter of considerable doubt. The amount of fat appearing in normal urine is, however, very small, even after a very abundant use of fat, as is shown by the very careful quantitative determinations made by Lang. This observer generally found no more than about 0·11% of fat in the solid residue of the urine of cats which had been fed on fatty flesh; in human urine he found, in one instance, 0·2% in the solid residue.

I have never observed true milky or chylous urine in which the turbidity and coloration were owing to fat. Urine of this kind owes its peculiarity to an excess of suspended pus-corpuscles, which, in all the cases hitherto observed, originated in the kidneys, and were not owing to vesical catarrh. Whenever this kind of milky urine is actually found to be rich in fat, it may be owing to the presence of milk added, as in Rayer's case,* for the sake of deceiving the physician. Bence Jones† has recently examined with care a case of this kind of chylous urine, and the following are the results at which he has arrived: the urine contained from 0·7 to 0·8% of fat, associated with which there were, however, also albumen, fibrin, and normal blood-corpuscles; the greatest amount of fat was found in the urine after digestion, although the blood was not found to be richer in fat.

Neither motion nor rest exerts any influence on the amount of fat in the urine, although it may affect the above-named abnormal constituents of that secretion. No change could be perceived in the kidneys (on dissection) by the naked eye, and they were not examined by the microscope.

(53) Addition to p. 427, line 27.—We have already spoken, in the first volume, of the amount of *sugar* in the urine under different physiological and pathological conditions. I must, however, here additionally remark that, contrary to my earlier experiments and the more recent observations of Uhle, sugar occasionally passes into the urine after the use of highly saccharine

* Traité des maladies des Reins. T. 1, p. 159.

† Philosophical Transactions. 1850, pp. 651-660.

food. C. Schmidt* had indeed made an experiment of this nature on a cat, and Bernard had been led from his observations to maintain a similar view, but the experiments made under my direction by Dr. von Becker were the first to convince me that under at least apparently similar relations, sugar is quite as often absent as present in the urine of rabbits after the use of highly saccharine food (carrots), or after the injection of solutions of sugar into the stomach of those animals. Certain relations which exert a general influence on the secretion of urine, appear, moreover, to exercise a special action on the urinary secretion. Thus Dr. von Becker observed in several experiments that rabbits, into whose stomachs a concentrated solution of sugar had been injected, did not exhibit sugar in the urine unless the urinary secretion was very abundant; these animals continued perfectly well even when as much as 60 grammes had been injected in the course of three hours. Other rabbits, however, which exhibited morbid symptoms, or which speedily died in consequence of excessive filling of the stomach and intestines (as far as the transverse colon) with saturated saccharine solutions, voided very little urine containing no sugar whatever. It would appear, therefore, that sugar does not readily pass into the urine when the quantity of the secretion is diminished. It is worthy of remark that only from 0·336 to 0·348% of sugar was found in the blood of those rabbits which retained their healthy appearance and liveliness, whilst as much as from 1·03 to 1·20% of sugar was found accumulated in the blood of those animals which apparently suffered after the injection of sugar, and which secreted only small quantities of urine that was either very poor in sugar, or entirely free from that substance. It would appear, therefore, that when the quantity of sugar in the otherwise normal blood exceeds 1%, the other limit is reached at which no sugar passes into the urine, and at the same time the urinary secretion is then reduced to the minimum.

(54) Note to p. 428, line 13.—[For much additional information on the *abnormal pigments* of the urine, we may refer to the Memoirs of Dr. A. H. Hassall,† read before the Royal Society, on June 16, 1853, and June 15, 1854, "On the frequent occurrence of indigo in human urine, and on its chemical, physiological, and pathological relations;" of Dr. Harley,‡ "On the colouring

* Charakter. d. Cholera. S. 167.

† Proceedings of the Royal Society. Vol. 6, p. 327, and Vol. 7, p. 122.

‡ Pharm. Journ. Nov. 1852.

matters of the urine;" of Virchow,* "On the pigments in the urine;" of Heller,† "On uroërythrin as a constituent of the urine in diseases;" and of Kletzinsky‡ "On uroglaucin, considered as an oxide of indigo."—G. E. D.]

(55) Addition to p. 445, 2 lines from the bottom.—The *volumetric method* is on many accounts to be preferred to determinations by weight, in the analysis of the urine. This method has not only the advantage over weighing of being more rapidly accomplished, which is especially desirable in the case of urine-analyses, in which, for the most part, a large series of observations are necessary for the attainment of reliable results, but it has the further advantage of rendering all long-continued evaporation unnecessary, and this is a great advantage, in consequence of the decomposition of the urine, which this process always induces. This method, after having been for a long time employed in testing metals, has been adopted by Liebig in the analysis of the organic juices. We have already considered in detail (vol. i, p. 287) Fehling's method of determining the sugar in the urine. The following method for determining the amount of *phosphoric acid* in the urine was recommended to Breed by Liebig.§ A solution of perchloride of iron, of definite strength, is added to acid urine, or to urine which has been acidified with acetic acid, until no more phosphate of iron is separated; the quantity of phosphoric acid in the urine is then calculated from the volume of the iron-solution which has been employed. The solution of the perchloride of iron is prepared by dissolving 15·556 grammes of iron in *aqua regia*, and then carefully evaporating the solution to dryness in a water-bath, in order to remove the excess of free acid without decomposing and volatilising any part of the perchloride of iron. The residue is dissolved in 2000 c.c. of water; 1 c.c. of this solution will precipitate 0·010 of a gramme of phosphoric acid (that is to say, 10 millegrammes). In the place of this solution we may employ one of undetermined concentration, the strength of which may be tested by a solution of phosphate of soda, whose amount of phosphoric acid has been previously determined. The solution of perchloride of iron must not, however, contain any of the protochloride. In order to ascertain whether

* Arch. f. pathol. Anat. Bd. 6, S. 259.

† Arch. f. Chem. u. Mikrosk. 1853, S. 361.

‡ Ibid. p. 414.

§ Ann. d. Ch. u. Pharm. Bd. 78, S. 150.

all the phosphoric acid has been precipitated, and there is a *trace* of perchloride of iron in excess, we must moisten a slip of paper saturated with ferrocyanide of potassium with a drop of the urine to be tested; if the excess is considerable it will be detected by the formation of Prussian blue. Here, as in all cases in which this method is employed, the quantity of the substance to be determined in a previously determined volume of the urine, is ascertained from the volume of the test-fluid which has been expended in the experiment.

We may proceed in a perfectly similar manner in the determination of the *chlorine* and *sulphuric acid* in the urine; but here we must acidify the urine with nitric or hydrochloric acid, and bear in mind that, notwithstanding the free acid, organic matter, combined with oxide of silver or baryta (as, for instance, uric acid, &c.), is precipitated, although perhaps only in very small quantities, together with the chloride of silver and sulphate of baryta, and hence rather more chlorine, and especially more sulphuric acid, is always calculated than the urine actually contains.

Liebig* has suggested a very ingenious method for determining volumetrically the amount of *urea* in the urine, which is closely connected with a chemical fact that he has recently discovered,† namely, that if bichloride of mercury in solution, and bicarbonate of potash in excess, be added to a solution of urea, we obtain a compound of urea and mercury, $\overset{+}{U} + 4\,HgO$, which is perfectly insoluble in water. This method has, further, this advantage, that we simultaneously determine the amount of *chlorine* in the urine. The following are the main steps in the process. In order to remove the phosphates and sulphates of the urine, a definite quantity of the fluid is mixed with half its volume of a fluid, containing 1 volume of a saturated solution of nitrate of baryta to 2 volumes of a saturated solution of caustic baryta. We take about 15 c.c. of the filtered alkaline fluid, (which consequently contains for every 3 volumes 2 volumes of urine), and then, without neutralising it, we add from a burette a solution of nitrate of mercury of known strength, as long as any precipitate is formed. The mixture must be well stirred during this process. The precipitate is the above-mentioned compound of urea and oxide of mercury, $\overset{+}{U} + 4\,HgO$. When a few drops of the turbid fluid are poured into a watch-glass, and one drop of a

* Ann. d. Ch. u. Pharm. Bd. 85, S. 289-328.

† Ibid. Bd. 80, S. 123.

solution of carbonate of soda is added, the mixture soon becomes yellow when treated with an excess of the solution of mercury, but it remains white when the solution of mercury is insufficient to precipitate all the urea. Very different methods may of course be employed for the preparation of the test-fluid (of nitrate of mercury); Liebig has, however, proposed a very simple method for this purpose, which consists in treating nitrate of mercury, in place of the bichloride, with phosphate of soda; if, however, a solution of common salt, of known concentration, be added to a mixture of these salts before the precipitate of the phosphate of mercury is rendered crystalline, the quantity of the oxide of mercury may be very easily calculated from the volume of the chloride of sodium necessary for its re-solution (for one equivalent of chloride of sodium necessarily corresponds to one equivalent of the phosphate of mercury). We may, however, at once obtain a solution of chloride of sodium suited for the purposes of these experiments, when we consider that a solution which is saturated between the temperatures of 0° and 100° constantly contains 27% of salt.

The method of determining the amount of *chlorine* in the urine is based upon the fact that, on the one hand, urea may be precipitated by the nitrate but not by the bichloride of mercury, and, on the other hand, that the nitrate becomes converted into bichloride of mercury when brought in contact with chloride of sodium. In order, therefore, to find the amount of chlorine in the urine, a definite volume of it should be decomposed with the solution of baryta; the urine which is filtered from the precipitate should then be treated with nitric acid until it is completely neutralised, and the solution of the nitrate of mercury poured upon it until the precipitate no longer dissolves on being stirred (that is to say, as long as bichloride of mercury is formed). The quantity of the bichloride of mercury, or of the chlorine, contained in the urine may be calculated from the volume of the solution of mercury which has been used.

The amount of the secretion of urine exhibits greater fluctuations than the secretion of any other organ. So many of the most varied external and internal conditions here come into play, that it would be impossible to estimate them perfectly, either for special or general cases. Although we may form to ourselves a tolerably correct idea of the more remote influences acting upon the secretion of urine, and of their extent, we are still very deficient in the knowledge of the more immediate conditions

which influence this secretion and regulate the variations in its amount. The science of physiology more especially feels the want of those chemical investigations, which might elucidate the relation of the character and composition of the blood to the secreted urine, although we are not deficient in isolated facts confirming the proposition which had been *à priori* advanced, that the constitution as well as the amount of the urine must depend upon the existing constitution of the blood. In the meanwhile it cannot be overlooked, that the chemical character of the blood cannot be the exclusive cause of all or any of the modifications in the urine, but that the mechanism of this secretion, as well as the condition of the nervous system, must be included amongst the immediate agents of the secretion of the urinary matters from the blood, and therefore must control the amount of the secretion. Whilst it is only recently that the view has been generally admitted, that the most essential constituents of the urine exist preformed in the blood, it has even been attempted to refer the process of the secretion to purely dynamical relations, depending upon the nervous system. No sooner was the fundamental law of endosmosis established, than it was supposed that the transmission of the urinary constituents into the "tubuli uriniferi" might be referred to this process; but a more thorough investigation of the laws of endosmosis sufficiently demonstrated that endosmosis alone was insufficient to afford an explanation of the mechanical processes involved in the secretion of urine. Ludwig* made the first successful attempt to establish a theory for the mechanical part of the process of the urinary excretion in the kidneys. Whichever view one may incline to in reference to the terminations of the urinary canals, it must be admitted that the principal part of the secretion from the blood is effected in those singular coils of vessels, the Malpighian bodies. It would appear, however, from the measurements of most histologists, that the capillaries leading from the Malpighian bodies are of a smaller diameter than the vessels constituting the bodies themselves; hence it follows from the laws of hydraulics that there must be a greater pressure against the walls of the latter, by which means, according to Ludwig, the water passes through them, and the true urinary constituents are introduced into the "tubuli uriniferi." The collected urinary fluid, which is so rich in water, is further impelled through the "canalicula contorta" by the fluid which is subsequently exuded from the blood; here, however, these small vessels are surrounded

* Handwörterb. d. Physiol. Bd. 2, S. 637-640.

by a network of vessels originating in the "vasa efferentia," and here an endosmotic interchange seems so far probable, that the more concentrated blood of the different vessels is necessarily brought into contact with the thin urinary solution, from which it again abstracts water, and thus leaves the urine more concentrated.

Ludwig advances the following grounds, in addition to the anatomical arrangement of the kidneys, in support of this view. According to him, his view explains why the urine never exceeds a certain degree of concentration; why a rapidly secreted urine is in general very much diluted, whilst urine which is more slowly secreted, is generally more concentrated; why the amount of urine increases as the quantity of the excretory matters of the blood is augmented; and finally, why no more fluid passes from the kidneys, after the solid constituents of the urine have been excreted in the kidney.

As Ludwig's whole theory rests essentially on the difference in the pressures of the blood, he has directed his attention to the more thorough elucidation of the influence of this relation upon the urinary secretion. Whilst Kierulf endeavoured, under his direction, to ascertain the influence of the character of the blood, especially its amount of water, Goll* made the mechanical question the subject of a series of very admirable observations. From his labours we may conclude with certainty, that the lateral pressure in the arterial system of the kidneys exerts a very important influence on the urinary secretion. Thus, for instance, on irritation of the nervi vagi, as well as when the vascular system is deficient in blood, that is to say, during conditions in which the tension in the arterial system is diminished, the urinary secretion was found to be very considerably diminished, whilst this secretion was greatly augmented during an increased tension of the blood in the arterial system, when this condition was induced by the tying of some of the larger arteries. It was further shown, that in addition to this well-attested influence of the pressure of the blood, other causes exerted a modifying action on the amount of the secretion. But as it was further proved, that even where the constitution and pressure of the blood were the same, the excretion of urine from the two kidneys was never parallel (for either the right or the left kidney secreted more than the other), other relations, as for instance, the influence of the kidneys upon the contractile fibres of the renal tissue, and the yet unknown relations of

* Ueber d. Einfluss des Blutdrucks auf. d. Harnabsonderung. Inaug.-Abd. der med. Fac. zu Zürich vorgel. 1853.

the constituents of the blood to the permeability of the walls of the blood-vessels and urinary canals will still have to be taken into consideration.

(56) Addition to p. 446, line 20.—Winter found that three youths discharged respectively the average quantities of 1672, 1702, and 1933 c. c. of urine in 24 hours, the extremes being 910 and 3340 c. c.

Scherer found that a child, aged three years and a half, discharged 755 grammes; a boy, aged seven years, 1077 grammes; a man, aged twenty-two years, 2156 grammes; and a man, aged thirty-eight years, 1764 grammes in 24 hours.

Now if we reduce these and certain other determinations to the weight of the body as a standard, it follows from Winter's experiments, that a man for every kilogramme's weight discharges an average quantity of 25·9 grammes of urine (the maximum being 46·8, and the minimum 14·0 grammes). According to Scherer, a child for every kilogramme's weight discharges 47·4 grammes, while the corresponding quantity in an adult is only 29·5 grammes; further (according to Schmidt)* a cat during an abundant flesh-diet (108·755 grammes of fatty meat) discharges in 24 hours 91·036 grammes of urine for every kilogramme of its weight; on a less abundant flesh-diet (44·118 grammes of meat) 53·350 grammes of urine; on 75·938 grammes of meat 71·570 grammes of urine; and on 46·154 grammes of meat (without any drink) 26·454 grammes of urine; a kitten which consumed daily 83·769 grammes of meat, discharged 60·455 grammes of urine.

(57) Addition to 448, line 12—According to Scherer's† determinations, a child, aged three years and a half, excreted in 24 hours 26·13 grammes of solid matter with the urine; a boy, aged seven years, 32·40 grammes; a man aged twenty-two years 47·97 grammes; a man aged thirty-eight years 71·23 grammes; and an insane patient, aged fifty years, who was starving himself, 23·69 grammes.

It is obviously to be expected, that the quantities of solid constituents which are separated by the kidneys should be very variable. Thus it is manifest, that whenever the metamorphosis of matter is more active than usual, and after the expenditure of bodily force, or an abundant supply of food (especially nitrogenous matters),

* Verdauungssäfte und Stoffwechsel. S. 304.

† Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 3, S. 280-290.

and in certain diseases associated with a considerable wasting of certain organs, the quantity of the matters excreted with the urine will be considerably augmented, without reference to the excretion of water. But further investigations are still required to elucidate scientifically the relations of dependence of the quantity of those substances on their original conditions, and more especially on the simultaneous physical and chemical constitution of the blood. The cases are far more frequent in which there is a diminution in the excretion of solid matters through the urine, as for instance in those diseases in which the metamorphosis of matter is either partially or generally altered. It is, therefore, in the latter cases especially that more frequent opportunities have presented themselves of gaining a more intimate knowledge of these conditions, and their direct and indirect effects. Thus, for instance, it has been generally found that in Bright's disease, the normal constituents decrease to an extraordinary degree, which may be readily explained by the loss of unchanged nutrient matters (albumen in this disease.) As soon, however, as a more active metamorphosis of matter is induced by the occurrence of febrile excitement or an inflammatory process, the constituents of the urine are again excreted in the normal, or in an increased quantity while there is at the same time a diminution of the albumen (Scherer.*) As we observe in Bright's disease, so also we learn from direct experiments, that after the artificial *augmentation of the salts of the blood, the normal constituents of the urine are considerably diminished.*

We may here add a few remarks on the recent investigations which have been made regarding the quantity of *urea* that is secreted under different conditions. According to Scherer's observations, a child excretes 0·810 of a gramme in 24 hours for every kilogramme of its weight, and an adult only 0·420 of a gramme; while, according to Schmidt, a cat when eating daily 108·755 grammes of fat meat, excretes 7·663 grammes of urea for every kilogramme of its weight; when taking 44·118 grammes of meat 2·958 grammes of urea; when taking 75·938 grammes of meat 5·152 grammes of urea; and when taking 46·154 grammes of meat 3·050 grammes of urea. Hence a cat living on a flesh-diet forms and separates by the kidneys on an average 6·8 parts of urea for every 100 parts of flesh which it consumes. If all the nitrogen of the food were separated as urea, rather more urea would of necessity be excreted than corresponds to the above mean numbers. For

* Pathologische Untersuchungen.

100 parts of flesh contain, according to Schmidt's analyses, 22·83 parts of muscular substance and tendon; and 100 grammes of albuminates + collagen = 16·11 of nitrogen (with 53·01 of carbon, 7·02 of hydrogen, 22·86 of oxygen, and 1·00 of sulphur); hence these 100 parts of nitrogenous matters must yield 34·52 parts of urea (which contain 16·11 of nitrogen). Hence 100 parts of flesh (corresponding to 22·83 of albuminates + collagen) yield according to this calculation 7·88 parts of urea. A cat during 18 days' inanition excreted on an average 2·11 grammes of urea in 24 hours for every kilogramme's weight.

With regard to the *extractive matters* Scherer found that a child aged three years and a half, excreted in 24 hours (when living on a mixed diet) 2·17 grammes of extractive matters; a boy, aged seven years, 3·88 grammes; a man, aged twenty-two, 24·335 grammes; a man, aged thirty-eight years, 20·484 grammes; and an insane patient, aged fifty years, who was starving himself, 10·59 grammes.

The *fixed salts* discharged with the urine in 24 hours, were determined by Scherer as follows: in the child, at 10·98 grammes; in the boy, at 10·23 grammes; in the young man, at 23·627 grammes; in the middle aged man, at 29·919; and in the man who was starving himself, at only 3·62 grammes.

In addition to what has been already remarked [partly in the text, and partly in the additions] regarding the individual amounts of the various organic matters, we have only to add, that according to the recent investigations of Hegar, Gruner, and Winter, an adult man excretes in 24 hours for every kilogramme of his weight 0·064 of a gramme of phosphoric acid, (the extremes being 0·096 and 0·043 of a gramme); and 0·032 of a gramme of sulphuric acid. According to Schmidt's investigations, a cat when living on 108·7 grammes of flesh excretes 0·267 of a gramme of sulphuric acid for every kilogramme of its weight; when living on 44·12 grammes of flesh, 0·106 of a gramme; when living on 46·15 grammes of flesh 0·084 of a gramme; and when living on 76 grammes of flesh 0·078 of a gramme.

END OF ADDITIONS AND NOTES TO VOL. II.

NOTES TO VOLUME III.

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(1) Note to p. 121, line 11.—[Von Bibra's Memoir is divided into nine sections, which treat respectively of:

I. The relative proportions of water, fat, and solid constituents in the brain of man and animals.
II. The fats of the brain.
III. The water-extract of the brain.
IV. The inorganic constituents of the brain.
V. The amount of phosphorus in the brain.
VI. The grey and white substance of the brain.
VII. The brain in insane patients.
VIII. The brain in the embryo and in extremely young animals.
IX. The weight of the brain as compared to that of the body.

I. From a very large number of analyses (he determined the amount of fats, water, and solid constituents in more than 100 cases in the human brain, in 138 other mammals, in 75 birds, and in 13 amphibians and fishes) he draws the following conclusions.

1. Within certain limits the quantity of fat is constant in the brain of man, as also in that of other animals.
2. Diseases of the general system, and even such as induce a diminution or disappearance of the fat in other parts, do not occasion a diminution in the amount of the brain-fat.
3. Fattening an animal appears to exert no special influence on the amount of fat in the brain.
4. The brain in other mammals contains less fat than the human brain. Where the opposite is the case, it appears to be induced by the ratio of the weight of the brain to that of the body, that is to say, the smaller quantity of cerebral substance is compensated for by a larger quantity of fat.
5. The brain in birds contains less fat than the brain in mammals.
6. The brain in amphibians and fishes contains a trace less fat than that of birds.

7. In man, other mammals, and birds, the medulla oblongata contains the largest amount of fat.

8. The quantity of fat in the hemispheres is both relatively and absolutely greater in man than in the other mammals, and in the latter than in birds.

9. The whole quantity of brain-fat in old men is a little less than that in adults in the prime of life.

10. The water and solid constituents (the fat not being included) fall and rise in their amount in all classes of animals with the augmentation or diminution of the fat, the albuminous matters being liable to the greatest variations.

11. It is not definitely established that the brain in mammals contains a larger mean quantity of water than the human brain; it would appear as if in this class of animals the smaller quantity of fat is compensated for by the albuminous substance rather than by water.

12. In birds, on the contrary, the amount of water in the brain is unquestionably larger than man or other mammals.

Von Bibra believes that the analyses, from which the preceding conclusions are drawn, establish beyond all question the importance of the fat in relation to the functions of the brain.

II. The brain-fats seem to have been submitted by him to a very careful investigation. The following are his chief conclusions. The brain-fats consist of cerebric acid and cholesterin, and of a series of fatty acids which possess very different properties and very diverse fusing points. These fatty acids are not the same in different brains even of one and the same species; and it would seem probable that in the living organism they are undergoing perpetual decomposition, passing into one another, and taking a share in the cerebral functions. They contain no nitrogen or sulphur, and those which solidify below—12·5° C., contain no phosphorus.

His cerebric acid agrees very well with the acid described by Fremy: von Bibra however finds as a mean of five analyses only 0·52% of phosphorus (the extremes being 0·49 and 0·55%), whereas Fremy fixed this constituent at 0·9%. He found that in adult men the brain-fat contains 20 or 21% of cerebric acid, and from 30 to 33% of cholesterin, while the remainder is made up of the above-noticed fatty acids and their salts.

The cerebric acid is rather more abundant in the brain of man than in that of the other large mammals.

The grey substance of the brair contains the least cerebric

acid, a mean quantity of cholesterin, and an excess of the other salts.

The white substance contains more cerebric acid and cholesterin than the grey, and consequently less of the other fats.

Although all these constituents of the brain-fat are found in the smaller mammals as well as in birds, amphibians, and fishes, and likewise in young infants and in the embryo, yet the quantity of cerebric acid seems to diminish as we descend the animal scale, and to be smaller in the infant and fœtus than in the adult.

III. His examination of the water-extract was not very satisfactory. He found

1. That the water-extract of the brain both of man and other mammals was entirely devoid of all those crystallisable bodies which have as yet been found in other parts of the organism.

2. That lactic acid was certainly present, and probably also another non-volatile acid, in addition to volatile acids.

3. That, besides albumen coagulable by heat, there were present various modifications of albuminous substances which were not precipitated from their solutions by boiling; and that at least two nitrogenous substances were present, one of which was soluble in water alone, the other in water and alcohol.

IV. From a large number of analyses of the mineral constituents of the brain he deduces the following conclusions:—

1. The inorganic constituents of the cerebral substance are the same as we meet with in other organs and in the formative fluids.

2. This qualitative condition holds good in all the classes of the vertebrata.

3. The ratio of the potash to the soda is nearly intermediate between the ratios occurring in the ashes of flesh and blood respectively.

4. Sulphates are almost entirely absent, and the quantity of the chlorine is very variable.

5. In man and other mammals the medulla oblongata contains more earthy phosphates than the other parts of the brain.

6. The amount of inorganic constituents is greater in the brain of birds than in that of man or other mammals.

7. The brains of amphibians and fishes contain more inorganic constituents than those of the other classes of animals.

8. The amount of earthy phosphates is moreover greater in the brains of amphibians and fishes than in the other classes of animals.

V. We quote the following determinations of the amount of phosphorus in human brain-fat.

Man aged 59 years. Bright's disease.
100 parts of fat from

The medulla oblongata contained		....	1·65	of phosphorus.
The cerebellum and Pons Verolii contained			1·83	„
The crura cerebri	„	....	1·76	„
The hemispheres	„	....	1·83	„
The corpora striata	„	....	1·65	„
The optic thalami	„	....	1·54	„
The corpus callosum	„	....	1·54	„
The mean for all the parts being	„	....	1·68	„

In a girl aged 19 years, the mean quantity was 2·53; in a man aged 65 years, who died from marasmus senilis, 1·72; in a man aged 80 years, who died from old age, 1·93; and in a man aged 25 years, 1·89.

In three cases of insanity, the patients being men of the respective ages of 36, 38, and 52 years, the percentage of phosphorus in the brain-fat was 1·75, 1·93, and 1·87.

Von Bibra draws the following conclusions from his numerous analyses:—

1. The amount of phosphorus in the brain-fat is very nearly the same in man, in other mammals, and in birds. With the exception of a single case, that of the chamois, in which it amounted to 3·40, it never exceeded 3·0%, and it never sunk below 1·0%, except in Falco nisus, in which it was as low as 0·72%.

2. The phosphorus in the brain-fat of insane persons does not exceed the mean amount; nor does extreme old age modify the quantity.

3. The brain in very young persons, and in the embryo, presents no peculiarity in this respect.

4. The fat of the grey matter contains rather more phosphorus than that of the white substance of the brain.

Von Bibra believes that the phosphorus of the brain belongs to one of the brain-fats, and in part unquestionably to the cerebric acid, and that consequently its amount varies in different brains with the amount of fat: there is, however, no reason to believe that there is any special connexion between the intelligence and the amount of phosphorus.

VI. The grey and white matter of the human brain were separately analysed by von Bibra. We quote his analysis in the case of a man aged 30 years, who died from pulmonary phthisis.

	(*a*) Grey substance of the hemispheres.	(*b*) White substance of the corpus callosum.	(*c*) White substance of the medulla oblongata.
Fat	6·43	20·43	14·67
Water	83·57	69·19	71·55
Solid constituents (exclusive of fat)	10·00	10·38	13·78

This brain-fat was again analysed, and found to be composed as follows:—

	(*a*)	(*b*)	(*c*)
Cerebric acid	2·64	20·72	24·70
Cholesterin	34·74	37·07	47·06
Other fats	62·62	42·21	28·24

Hence it follows that the grey substance contains less fat than the white, and that the fat is here replaced by water: and further, that the cerebric acid, and to a certain extent the cholesterin, preponderate in the white substance.

VII. In the analyses of various parts of the brain of three insane persons he was unable to detect any striking chemical peculiarity.

VIII. We give his analyses of the brain of the human embryo at different stages, and of that of a child aged 6 months.

	At 10 weeks.	At 12 weeks.	At 14 weeks.	At 18 weeks.	At 20 weeks.	At 21 weeks.	At 37 weeks.	Child.
Fat	1·26	0·99	1·53	1·06	1·07	1·23	3·06	6·99
Water	85·10	86·71	86·24	86·90	86·03	85·93	87·90	82·96
Solid constituents (exclusive of fat...	13·64	12·30	12·23	12·04	12·60	12·84	9·04	10·04

From these and similar observations on the lower animals (dogs, cats, pigs, horses, goats, and cows), it appears that the amount of fat in the brain of the fœtus is far less than in that of the adult individuals, the difference being made up by an excess of water. The great and sudden augmentation of fat towards the end of fœtal existence, and shortly after birth, is a fact of much physiological interest.

The last section of von Bibra's Memoir pertains rather to Anatomy than to Chemistry, and therefore requires no notice in the present place.—G. E. D.]

(2) Note to p. 334, line 21.—[Dr. Reuling* has recently published a prize essay on the amount of ammonia in the expired air both in health and in disease, with especial reference to uræmia. The following are his most important conclusions:—

1. The exhaled air of every one contains ammonia.

2. In health its quantity depends on the amount of ammonia in the inspired air.

3. In healthy men there is neither an absorption nor an elimination of ammonia by the pulmonary mucous membrane.

4. Fresh normal human blood contains no ammonia; but almost immediately after it has ceased to circulate in the vessels (whether obtained by venesection or from the dead body), carbonate of ammonia and other ammoniacal compounds begin to be formed in it.

5. Logwood paper is the most sensitive of all the tests for ammonia, and detects it when diluted 64 million times.

6. The amount of ammonia in the expired air is *sometimes* increased in the following diseases:—In caries of the teeth, in angina tonsillaris, in typhus (in consequence of the formation of ammonia in the blood), in pyæmia (when ammonia is formed in the blood through the influence of pus), and in uræmia (either when ammonia is developed in the blood from the retained urea, or when the ammonia formed in the bladder from urea is taken up into the blood).

7. In all probability the amount of ammonia in the expired air is sometimes also increased in cholera and scarlatina.

8. The augmentation of the quantity of ammonia in the expired air occurs most frequently in uræmia, but is not a pathognomonic symptom of this disease.

9. The appearance of ammonia in the blood is certainly the most frequent, although it is not the sole cause of uræmia. Uræmia may be produced by the accumulation of the extractive matters in the blood in cases of suppression of urine.—G. E. D.]

(3) Note to p. 381, line 11,—[Dr. Malcolm † has just published

* Ueber den Ammoniakgehalt der expirirten Luft, und seiner Verhalten in Krankheiten. Ein Beitrag zur Kenntniss der Uræmie. Giessen, 1854.

† Dublin Quarterly Journal of Medical Science. Vol. 18, p. 320.

"Some experiments on the proportion of carbonic acid exhaled in phthisis pulmonalis." Fifteen patients, nine males and six females, in decided consumption, were operated on thirty-two times. The disease had reached the stage of softening in all but one, and in three there were cavities; the pulse averaged 104, the respiration 30. The result of the experiments in these cases was this: the percentage of carbonic acid averaged 4·467, the extremes being 3·7 and 5·5. The result of experiments similarly made upon twelve healthy individuals, six males and six females, at an average age of 29, showed an average percentage of 4·6916, ranging from 4·2 to 5·9.—G. E. D.]

(4) Note to p. 427, line 2.—[A memoir has just appeared by Drs. Falck* and Scheffer, "On the metamorphosis of matter during the deprivation of water," which I have not had an opportunity of consulting. An abstract of it is given by Dr. Weber, in his "Annals of Physiology," in the British and Foreign Medico-Chirurgical Review, vol. 14, p. 253.—G. E. D.]

* Arch. für physiol. Heilk. Bd. 13, S. 61.

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